

Fully matured abscess of forearm, which has become well-localized (upper figure). The streaking due to the lymphangitis has faded but the lymphoedema surrounding the inflammatory area remains. The skin in the centre is thin and shiny and its color has changed from a bright red to bluish. The pointing of the abscess is noted by the appearance of a yellowish spot in the centre of the shiny area. Insert *a*. Showing the abscess cavity being packed with gauze after the abscess has been incised and the pus within its cavity evacuated. Insert *b*. Cross-section of the abscess cavity packed with gauze to prevent pocketing and the accumulation of pus.

INTERNATIONAL CLINICS

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PATHOLOGY, DERMATOLOGY, OPHTHALMOLOGY,
OTÓLOGY, RHINOLOGY, LARYNGOLOGY,
HYGIENE, AND OTHER TOPICS OF INTEREST
TO STUDENTS AND PRACTITIONERS

BY LEADING MEMBERS OF THE MEDICAL PROFESSION
THROUGHOUT THE WORLD

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	PAGE
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BALFOUR, DONALD C., M.D., Division of Surgery, Mayo Clinic, Rochester, Minnesota	289
BRICKNER, WALTER M., M.D., F.A.C.S., Attending Surgeon to the Broad Street Hospital, New York City	207
CATTELL, HENRY W., A.M., M.D., Fellow of the Philadelphia College of Physicians; Lieutenant-Colonel, Medical Reserve Corps, U. S. A., Etc., Philadelphia	222
COUPAL, JAMES F., M.D., Major, Medical Corps, U. S. A., Washington, D. C.	222
CUSHING, H. B., M.D., Professor of Pædiatrics at McGill Medical College; Physician to the Royal Victoria, Children's Memorial, and Alexandra Hospitals, Montreal, Canada	1
DEKRAFT, FREDERIC, M.D., Consulting Electrotherapeutist to the Manhattan State Hospital and the Reconstruction Hospital, New York City.....	92
GWYN, NORMAN B., M.B., Senior Demonstrator in Medicine, University of Toronto Medical Faculty; Assistant Physician to the Toronto General Hospital, Toronto, Ontario	136
HENDRICKS, WILLIAM A., M.D., Fellow in Surgery, Mayo Clinic, Rochester, Minnesota	177
HORGAN, EDMUND, M.D., F.A.C.S., Attending Surgeon to the Children's Hospital, Washington, D. C.	189
JOURDA, L. M., M.D., Faculty of Medicine of Toulouse, France	44
KRAEPELIN, Professor E., Deutsche Forschungsanstalt für Psychiatrie, Munich, Germany	52
LAROQUE, G. PAUL, M.D., F.A.C.S., Associate Professor of Surgery, Medical College of Virginia, Richmond, Virginia	25
MASON, EDWARD H., M.D., Assistant Director, University Clinic, McGill University and the Royal Victoria Hospital, Montreal, Canada	163
MILCH, HENRY, M.D., Assistant Surgeon to the Broad Street Hospital, New York City	207

MILLER, C. JEFF, M.D., F.A.C.S., Professor of Obstetrics and Gynæcology, Tulane University, New Orleans, Louisiana.....	120
MUIR, JOSEPH, M.D., Member of the Electrotherapeutic Society, New York City	112
NASSAU, CHARLES F., M.D., LL.D., Surgeon to Jefferson Hospital, Pihladelphia	199
PLAUT, Professor F., M.D., Deutsche Forschungsanstalt für Psychiatrie (Kaiser Wilhelm Institute), Munich, Germany.....	63
REID, J. SPENCE, B.A., M.B. (Toronto), Fellow in Surgery, the Mayo Founda- tion, Rochester, Minnesota	289
REIFENSTEIN, EDWARD C., M.D., Professor of Clinical Medicine, Syracuse University, Syracuse, New York	7
SNOW, WILLIAM BENHAM, M.D., Ex-president of the American Electrothera- peutic Society; Editor of the <i>American Journal of Electrotherapeutics</i> and <i>Radiology</i> , Etc., New York City	101
WEBER, F. PARKES, M.D., F.R.C.P., Senior Physician to the German Hospital, London, England	126

CONTENTS OF VOLUME I

(THIRTY-SIXTH SERIES)

DIAGNOSIS AND TREATMENT		PAGE
THE SEQUELÆ OF DIPHTHERIA. By H. B. CUSHING, M.D., of Montreal, Canada		1
THE DIAGNOSIS AND TREATMENT OF CARDIAC ARHYTHMIAS. By EDWARD C. REIFENSTEIN, M.D., of Syracuse, New York.....		7
THE TREATMENT OF APPENDICITIS. By G. PAUL LAROQUE, M.D., F.A.C.S., of Richmond, Virginia		25
BLOOD DILUTION IN THE PATHOLOGY AND TREATMENT OF ATTACKS OF GOUT. By L. M. JOURDA, M.D., of Toulouse, France.....		44
THE DEVELOPMENT OF PSYCHIATRICAL RESEARCH. By Professor E. KRAEPELIN, of Munich, Germany		52
THE TREATMENT OF METASYPHILITIC DISORDERS OF THE NERVOUS SYSTEM WITH INFECTIOUS DISEASES, IN PARTICULAR WITH RELAPSING FEVER. By Professor F. PLAUT, M.D., of Munich, Germany		63
THE MOTIONS OF THE LARGER JOINTS. By ASTLEY P. C. ASHHURST, M.D., of Philadelphia		74

ELECTROTHERAPEUTICS AND PHYSIOTHERAPY

THE CLINICAL ACTION OF DIATHERMY. By FREDERIC DEKRAFT, M.D., of New York City	92
TREATMENT OF LOCAL INFECTION. By WILLIAM BENHAM SNOW, M.D., of New York City	101
RADIOTHERAPY OF THE BLOOD AND LYMPH-TISSUES. By JOSEPH MUIR, M.D., of New York City	112
CONTRA-INDICATIONS TO THE USE OF RADIUM IN GYNÆCOLOGY. By C. JEFF MILLER, M.D., F.A.C.S., of New Orleans, Louisiana.....	120

MEDICINE

PARAPLEGIA IN LYMPHOGRANULOMATOSIS MALIGNA (HODGKIN'S DISEASE) AND LEUKÆMIA, AND THE QUESTION OF THERE BEING A "HODGKIN SARCOMA" AS WELL AS A "HODGKIN GRANULOMA." By F. PARKES WEBER, M.A., M.D., F.R.C.P., of London, England	126
MASSIVE COLLAPSE OF THE LUNGS. By NORMAN B. GWYN, M.B., of Toronto, Canada	136
THE LIFE HISTORY OF A CASE OF NEPHROSIS. By EDWARD H. MASON, M.D., of Montreal, Canada	163

SURGERY

A DAY IN DR. CHARLES H. MAYO'S CLINIC. By WILLIAM A. HENDBICKS, M.D., of Rochester, Minnesota	177
DIAGNOSIS AND TREATMENT OF ACUTE SUPERFICIAL CIRCUMSCRIBED ABSCESS. By EDMUND HORGAN, M.D., F.A.C.S., of Washington, D. C.	189
THE SURGICAL TREATMENT OF GASTRIC AND DUODENAL ULCERS. By CHARLES F. NASSAU, M.D., LL.D., of Philadelphia.....	199
SURGICAL CLINICS FROM THE BROAD STREET HOSPITAL, NEW YORK. By WALTER M. BRICKNER, M.D., F.A.C.S., and HENRY MILCH, M.D., of New York City	207

PROGRESS OF MEDICINE FOR 1925

COLLATION. By HENRY W. CATTELL, A.M., M.D., of Philadelphia, and Major JAMES F. COUPAL, M.D., of Washington, D. C.	222
RECENT PROGRESS IN SURGERY. By DONALD C. BALFOUR, M.D., and J. SPENCE REID, B.A., M.B. (Tor.), of Rochester, Minnesota	289
CUMULATIVE INDEX	305

LIST OF ILLUSTRATIONS TO VOLUME I

(THIRTY-SIXTH SERIES)

COLORED PLATE

PAGE

Fully matured abscess of forearm, which has become well-localized (Fig. 1)	Frontispiece
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PLATES, CHARTS AND FIGURES

Course of events in a typical case of diphtheria, in a child, aged five years, treated with serum; graphically illustrated (Fig. 1)	5
Schematic diagram to illustrate the location of the S.-A. Node; the A.-V. Node; the bundle of His with the right and left branches; as well as the possible site of impulse formation of various premature beats (Fig. 1)	16
Premature auricular beats showing inverted P. in leads II and III (Fig. 2)	17
Auricular tachycardia, lead I (Fig. 3)	16
Premature ventricular beats (Fig. 4)	17
Continuous lead. Premature ventricular beats showing interpolated beats. This patient had not received any digitalis (Fig. 5)	20
Continuous lead. Premature ventricular beats showing interpolated beats. This patient had not received any digitalis (Fig. 6)	21
Continuous lead. Premature ventricular beats showing interpolated beats. This patient had not received any digitalis (Fig. 7)	22
Auricular flutter. Note the regularity of the auricular contractions with a 4 to 1 block. (Fig. 8)	23
Auricular fibrillation. Note the absence of "P" waves, presence of "F" waves with irregular ventricular responses (Fig. 9)	22
Auricular fibrillation. Note the absence of "P" waves, presence of "F" waves with irregular ventricular responses (Fig. 10)	23
Auricular fibrillation after digitalization. Note the absence of "P" waves, presence of "F" waves with irregular ventricular responses (Fig. 11)	22
Heart-block. Complete disassociation of the auricle and ventricle (Fig. 12)	23
Heart-block with auricular fibrillation. Note the absence of "P" waves, presence of "F" waves with regular ventricular complexes (Fig. 13) ..	22
Heart-block, auricular fibrillation and premature ventricular beats (Fig. 14) ..	23
A straight line is 180°; this corresponds to the fully extended position of a joint (as the elbow); flexion to a right angle is 90° flexion; flexion less than this (135°) and more than this (45°) are shown in the diagram (Fig. 1)	75
Goniometer indicates elbow flexion to 90° (Fig. 2)	75
Goniometer indicates flexion of hip to 135° (Fig. 3)	75
Flexion of shoulder to 90°, the normal limit (Fig. 4)	77
Extension of shoulder to 250° (70° back of the "anatomical position" of 180°) (Fig. 5)	77
Flexion of shoulder to 135° (Fig. 6)	78

Extension of shoulder to 200° (Fig. 7)	78
Abduction of shoulder to 45° (Fig. 8)	78
Abduction of shoulder to 90° (Fig. 9)	78
Elevation of arm above horizontal is secured only by rotation of scapula on chest (Fig. 10)	79
If ankylosis of shoulder exists, abduction even to 90° is secured only by rotation of scapula (Fig. 11)	79
Adduction of shoulder (Fig. 12)	79
External rotation of left shoulder to 90°; of right shoulder to 45° (Fig. 13)	80
External rotation of shoulder with abduction to 90° (Fig. 14)	80
Internal rotation of shoulder with abduction to 90° (Fig. 15)	80
Flexion of elbow to 30° (Fig. 16)	81
Extension of elbow to 180° (Fig. 17)	81
Hyperextension of elbow to 195° (Fig. 18)	81
Forearm in full supination, reckoned as 180° by indicator of pronometer (Fig. 19)	82
Forearm pronated to 90° (Fig. 20)	82
Flexion of wrist to 90° (Fig. 21a)	82
Hyperextension of wrist to 250° (Fig. 21b)	82
Abduction of wrist to 15° (a). Adduction of wrist to 45° (b) (Fig. 22) ..	83
Flexion of hip to 45° (Fig. 23)	83
Apparent flexion of hip to normal limit, but secured only by flexing the pelvis on the lumbar spine, as indicated by the other limb rising from the table (Fig. 24)	84
Hyperextension of hip to 190° or 200° (10° or 20° extension beyond the neutral position of 180°) (Fig. 25)	84
Loss of normal extension in the left hip (as from psoas abscess) demonstrated by hanging both lower extremities over the end of the table. The normal (right) hip goes into hyperextension (Fig. 26)	85
Adduction of left hip to 35° (Fig. 27)	85
Abduction of both hips to their normal limit (each at angle of 45°) (Fig. 28) ..	86
Adduction of the flexed (left) hip (Fig. 29)	86
Abduction of the flexed (left) hip (Fig. 30)	86
External rotation (60°) of the right hip (Fig. 31)	87
Internal rotation (30°) of the right hip (Fig. 32)	87
External rotation of flexed (right) hip to 80° (normal limit about 90°) (Fig. 33)	87
Internal rotation of flexed (right) hip to 210° (30° beyond sagittal plane) (Fig. 34)	87
Both knees flexed and hanging vertical: If hip were fixed in ankylosis in internal rotation, the leg would deviate away from its fellow; if in external rotation the reverse would be noted (Fig. 35)	88
External circumduction of right hip (Fig. 36)	88
Internal circumduction of right hip (Fig. 37)	88
Flexion (dorsi-flexion) of ankle to 70° (Fig. 38)	90
Extension (plantar flexion) of ankle to 135° (Fig. 39)	90
Pronation of the foot (valgus position) (Fig. 40)	91
Supination of the foot (varus position) (Fig. 41)	91

Microscopic appearance of the great mediastinal tumor, magnified 240 times (Fig. 1)	134
Tumor under still higher magnification (500 times) (Fig. 2)	134
Complete collapse of both lungs from impaction of food particles in bronchus (Fig. 1)	160
Microscopical section of lungs pictured in Fig. 1 (Fig. 2)	160
Collapse of the left base in association with pneumonia. The deviation of the mediastinum and heart to the left is apparent, the remarkable degree of falling in of the chest and obliquity of the ribs which represents the attempt to compensate for the collapse is well known. There is no scoliosis (Fig. 3)	161
Solid collapse of the right lung as a post-operative accident; the heart has practically disappeared into the right chest (Fig. 4)	160
The collapse is beginning to disappear, expanding lung to the extreme right margin of remaining collapse, replacement of mediastinum (Fig. 5) ..	161
Eventual replacement of mediastinum as lung clears, some signs of the collapse process still in evidence as diffuse shadows (Fig. 6)	160
A very complete picture of acute massive collapse of the right lung after operation. The falling of the ribs is evident; the heart and mediastinum are completely displaced into the consolidation (Fig. 7)	161
The same lung resolved; no full size plates were at hand at the time of taking these pictures; the heart shadow is seen to the left (Fig. 8)	160
This section of lung shows complete collapse of the alveoli in most of the section and partial collapse in the rest. The capillaries of the alveolar walls are all engorged with red blood-cells. There is no evidence of an inflammatory reaction. The bronchioles show a partial collapse and for the most part are filled with red blood-cells and a few wandering cells. The blood-vessels throughout appear normal (Fig. 9)	161
Avian tuberculosis of the spleen in man showing tubercles with a few foreign-body giant-cells, numerous large epithelioid cells and waxy substance in the centre (Fig. 1)	178
High magnification of one of the tubercles shown in Fig. 1 (Fig. 2)	178
Conglomerate tubercle in the liver of a fowl showing numerous large epithelioid cells (Fig. 3)	178
The external surface of the spleen presenting numerous nodules varying from 1 mm. to 2 cm. in diameter (Fig. 4)	179
The short dotted line represents the site of a posterior gastro-enterostomy; the long dotted line is the line of division of the stomach for resection (Fig. 1)	202
The line of division for resection when there is extensive induration of the duodenum; modified from Balfour (Fig. 2)	203
The Balfour anastomosis. Approximation of a sixteen-inch loop to the end of the stomach and in front of the colon with the posterior suture begun before the stomach is resected. The part of the stomach to be resected is held to the left. The first row of sutures is placed before the stomach is removed (Fig. 3)	202
Patrick M. Metastatic carcinoma of the humerus producing pathological fracture. Note that the growth appears quite circumscribed. There is bone absorption but no bone production, bone expansion, periosteal growth or cystic degeneration (Fig. 1)	208

Patrick M. Röntgenograms of the same growth two weeks later, after removal with some of the attached soft parts. The second picture shows the growth split open. Note the rapid extension of bone destruction almost to the articular surface (Fig. 2)	209
Patrick M. Osteoperiosteal transplant from tibia to replace resected portion of humerus (Fig. 3)	208
Patrick M. Carcinomatous obstruction of the thoracic œsophagus (Fig. 4)	209
Reproduction of original X-ray negative of hand, with ring on finger (Fig. 1)	222
Positive print from unretouched negative as received by telephone wire in Chicago from New York (Fig. 2)	223

Diagnosis and Treatment

THE SEQUELÆ OF DIPHTHERIA *

By H. B. CUSHING, M.D.

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OF ALL the acute infectious diseases of childhood, diphtheria is the one concerning which we have the most accurate knowledge. Not only are we thoroughly familiar with the cause, symptoms and course of the disease, but we have at our command efficient methods for diagnosing the disease, curing it, preventing it and, in short, for absolutely eradicating it in any civilized country. In other words, diphtheria has no license for existing or for having a death-rate. In spite of all this, diphtheria is still one of the chief causes of death among young children and is the third most important cause of death in children under five years of age in this country, only diarrhœa and pneumonia are more common. This being so, one may be excused for spending a little time enquiring into the causes of these deaths and be sure of discussing a subject of importance to everyone.

Children with diphtheria die from two causes, broadly speaking. They either suffocate from membrane in the larynx or lungs, or they die from the effects of the diphtheria toxin on the organs of the body. I have not time to-day to consider the first cause of death, but wish to speak only of the effects caused by diphtheria toxin. Diphtheria is a local disease, toxin is produced at the site of the lesion, usually in the throat, absorbed and acts on the various organs. It is a slow poison, taking some weeks to produce all its effects. The dose of the poison any given case has received when it first comes under observation can be approximately estimated by the extent of the local lesion and its duration before antitoxin is administered. An adequate dose of antitoxin prevents any further damage, neutralizes any toxin in circulation, or which may be produced later, but is of no avail in counteracting the toxin already absorbed and fixed in the tissues.

* Read before the Interstate Post-graduate Assembly, St. Paul, October, 1925.

There is a prevalent impression that the action of the toxin is most uncertain, causing heart failure in one patient, nephritis in a second, bizarre forms of paralysis in a third, and so on without any definite rule or reason. This is not so; if one observes carefully a large series of cases, one finds it possible to estimate, as I have indicated, the approximate dose of toxin received and to prophesy more accurately than in most diseases the subsequent course of events. The action of the toxin is surprisingly uniform, and although naturally one individual differs from another in his resistance and reaction, still the after-effects of a severe attack of diphtheria are remarkably similar in all cases.

Let us consider these effects more in detail. For clinical purposes, diphtheria affects three organs only, the kidneys, the heart and the nervous system. It may affect others, presumably does so. In fact, from autopsy findings and animal experiments, it probably affects the thyroid, liver, pancreas, and especially the suprarenals. But so far as our present means of observation go, we have no facility for accurately estimating the damage to these organs, and the effects on them do not apparently influence the clinical picture. Let us confine ourselves then to the three organs which give obvious clinical signs or symptoms.

The first evidence of the effect of the diphtheria toxin is from the kidneys in the form of a nephritis. This is a pure degenerative nephritis, manifesting itself at the end of a week or earlier by the presence of albumin and casts in the urine, usually in considerable quantity. This nephritis is almost constant after diphtheria, quite constant in all severe or late cases, causes a diminution in the amount of urine passed but never causes dropsy or uræmia or even serious retention of nitrogen or chlorides in the blood. True inflammatory nephritis after diphtheria with general œdema or uræmic symptoms means either an error in diagnosis or a mixed infection and is not due to the diphtheria toxin. The form of nephritis which one sees almost constantly after diphtheria is purely toxic, with degeneration and desquamation of the epithelial cells lining the tubules. It does not cause marked symptoms and always disappears entirely in a few weeks, leaving no after-effects. In many thousand cases observed in the Alexandra Hospital, Montreal, over a term of years, I can only recall a very few leaving the hospital with any signs of nephritis,

and in all these there was reason to believe that nephritis was present before the diphtheria or was due to some other cause than diphtheria alone. If the nephritis is so benign and transitory, is it of any clinical significance? Apart from influencing our treatment as regards diet during the first three weeks, I firmly believe it is of little importance beyond being a practical indicator of the amount of intoxication and hence of what may be expected from the other organs.

One wishes devoutly that the same could be said of the next organ to be involved, almost simultaneously with the kidneys, and that is the heart, the commonest cause of death in the fatal cases of diphtheria. Cardiac failure after diphtheria has always attracted much clinical interest, and varied have been the opinions as to its cause. Thrombosis, paralysis and vasomotor failure have all been blamed, and it is only since the work of Warthin and others in this country within recent years that the condition has been placed on a sound pathologic basis. We know now that the post-diphtheritic cardiac symptoms are due to an acute degenerative myocarditis. It is a toxic parenchymatous degeneration or necrosis of the muscle-fibres of the heart, with a later reparative inflammatory process with regeneration of the muscle. Both the contractile and conducting mechanisms of the heart may be affected by these processes. The occurrence of this myocarditis is apparently as constant as the nephritis, though it is harder to demonstrate. Only through change in the color of the patient, and in the character of the pulse does one suspect its presence in mild cases. Blood-pressure records help little nor does the electrocardiograph until the condition is well established. Cardiac dilatation with vomiting, heart-block or sudden death terminate the picture in the worst cases. The symptoms of myocarditis show themselves first on the fifth to the seventh day, culminate on the tenth to fourteenth day, and rapidly subside, although it is several weeks before the heart returns to normal. Still, if the twenty-first day is passed, one should no longer fear absolute cardiac breakdown, if reasonable precautions are taken. It is of great interest to know what becomes of these severely affected hearts later. Are they permanently crippled, does the degenerative myocarditis lead to a fibrosis in later life? I can only say that I have been interested in following a number of the worst of these cases, which unexpectedly survived after being pulseless and with signs of cardiac dilatation, and in no single case

was I able to demonstrate after one year that there was any disability whatsoever remaining, either by functional tests, physical examination or electrocardiographs. It is my firm belief that once the patient survives the acute attack there is absolute restoration of the heart to normal. I must confess that I am speaking only of children, and that it is possible that in adults the reparative power of the tissues may not be so great.

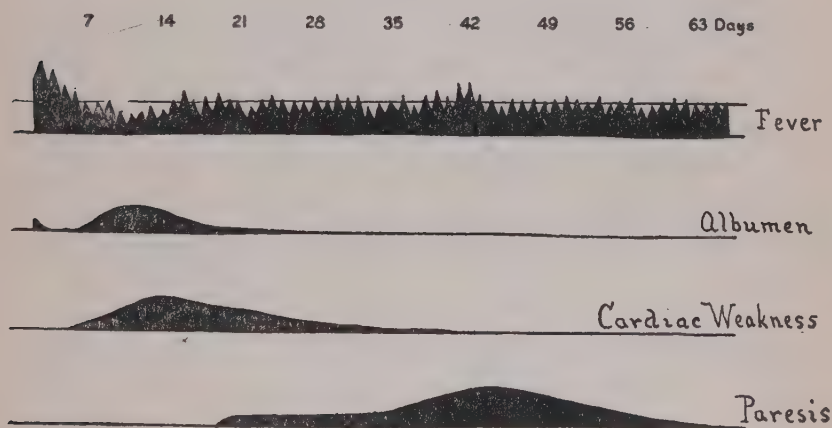
If, then, the outlook is so bright if the critical two weeks are survived, are there any therapeutic means of assisting the patient through this period? The only adjuvant I have any faith in is absolute physical rest in whatever way it may be secured. The patient should not be permitted to raise an arm from the bed; if vomiting begins, all nourishment by mouth should be stopped for two or three days. Morphine is given if there is restlessness, though this rarely occurs until the case is beyond hope, but rather a lassitude and somnolence. Digitalis does harm by increasing the tendency to vomiting and to heart-block, and other so-called "cardiac" stimulants seem of little avail. Remember always that it is only a few days to be survived and then the natural processes of repair will affect a cure.

The third clinical manifestation of the toxin, the effect on the nervous system, is always fascinating to watch. Until Walshe in England gave us the clue to these curious paralyses they seemed utterly irregular, purposeless and fantastic. Walshe showed clearly how the first effects on the nervous system were local, the toxin apparently passing along the local nerves from the site of the lesion to the central nervous system, affecting first the local nerves, then the neighboring nuclei and then the general nervous system as a whole. So in the ordinary pharyngeal cases of diphtheria there is first a paralysis of the soft palate, then two or three weeks later of the eyes and almost immediately after a weakness of all the body muscles with loss of tendon reflexes. If the diphtheria occurred in a wound of the leg, there would be paralysis of the leg first. So constant is this sequence that I have more than once observed in cases of diphtheria of one tonsil only that there was paralysis only of that half of the palate. The local paralysis is seen usually in the third week if closely looked for. The general paralysis begins about two weeks later with general weakness, paralysis of accommodation, squint, sen-

sory disturbances and loss of reflexes. It culminates almost invariably at the end of six weeks and then rapidly and steadily improves. The prognosis as regards life depends entirely on the involvement of the diaphragm and muscles of respiration. Fortunately these muscles are the last involved and their paresis is short-lived. If one can keep the patient alive for a week, all symptoms will subside, for in this, as in all other toxic sequelæ of diphtheria, recovery is absolute and complete in the process of time.

Fig. 1 illustrates graphically the course of events in a typical case of diphtheria, treated late with serum. One sees the immediate

FIG. 1.



John D. - 5 years - Diphtheria.

improvement and subsidence of all the evidences of the disease, so that the patient appears convalescent. Then the quickly developing evidence of the later action of the toxin; the appearance of albumin, rapidly increasing in amount and later disappearing entirely; the progressive impairment of the heart culminating in ten days, when the patient hovered between life and death for a few days, with sub-normal temperature and almost imperceptible pulse; lastly the paralysis beginning locally at the end of three weeks, becoming generalized in two weeks more, so that the patient passed through another critical period at the end of the sixth week and barely survived a threatened

respiratory paralysis and finally recovered entirely with apparent complete restoration to normal. This chart might be repeated in hundreds of other cases, differing only in the degree of the various symptoms caused by the toxæmia, for, as stated previously, one of the most striking things about the effects of diphtheria is the uniformity of the symptoms caused by the action of the toxin.

If this progressive clinical picture be a true one, what practical lessons may be drawn from it? First and foremost, the importance of early treatment, of an adequate dose of antitoxin at the earliest possible moment, by a route through which it has the most rapid action, *i.e.*, intravenously in all cases in which one has reason to suspect a dangerous dose of the toxin to have been absorbed. Secondly, the need of close observation of the patient, noting first the albuminuria giving a rough measure of the intoxication, second, the evidences of involvement of the heart-muscle and, lastly, the progressive involvement of the nervous system. The final lesson is the hope of the absolute restoration of the body to normal if the two brief critical periods can be survived; the one at the end of two weeks from cardiac failure and the other at the end of six weeks from respiratory paralysis.

THE DIAGNOSIS AND TREATMENT OF CARDIAC ARRHYTHMIAS *

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CARDIAC arrhythmias occur very frequently in practice. For some of these arrhythmias there is definite and specific therapy, while others are made worse by improper and useless medication. It is obvious, then, that for a proper appreciation of their significance, knowledge of the various conceptions as to the nature of the disturbance of the cardiac mechanism is necessary if intelligent treatment is to be prescribed.

Of prime importance in the study of disorders of rhythm is a knowledge of the impulse formation of the heart and its pathway through it. A brief review of the physiology of the conduction system may prove helpful. Some years ago, Keith called attention to the sinus region of the heart situated in the posterior portion of the right auricle, bounded above by the superior vena cava and below by the coronary sinus. Lewis named this region the pacemaker of the heart. Here are found peculiarly specialized muscle-fibres and nerve-cells. This tissue or node, the sino-auricular node, as it is called, is under the influence of the vagus and sympathetic nervous systems. The influence of the vagus on the heart is better understood than that of the sympathetic. Studies upon the vagus control of the heart have given us much information. It is the inhibitor of heart action and therefore slows the heart. Its tone is unstable before adolescence. Vagus tone is lessened by fever, exercise, and atropine. When one considers its origin in the brain and its wide distribution to various viscera, one will then appreciate the importance of reflex disturbances affecting the vagus control.

The sino-auricular node or pacemaker, as it is called, produces rhythmic impulses faster than other areas of rhythmic impulse formation in the heart, and therefore it dominates the rhythm of the

* Read before the combined meeting of the Tompkins and Cortland County Medical Societies, in June, 1925, and the Syracuse Academy of Medicine, October, 1925.

heart. If, for various reasons, other areas become more active, or the S.-A. node becomes depressed, then the impulse formation is taken over by one of these areas until the sino-auricular node can re-assert itself. As the impulse leaves the S.-A. node, it passes rapidly over the auricle to another area of specialized tissue, the auriculo-ventricular node. The impulse passes more slowly through this tissue and finally into another bundle of tissue, the bundle of His, which then divides into a right and left branch, finally ending in the special nerve-cells of Purkinje.

It is important to recognize sinus arrhythmia. It has certain characteristics and usually occurs in childhood or young adult life. It is apparently related to respiration but may occur independently of it. It may be brought on by digitalis therapy. The heart will be slow and at various times there will be detected cycles of different lengths, sometimes related to respiration and sometimes not. The irregularity may be abolished by atropine, exercise, and will disappear during a febrile attack, only to re-appear after the fever has gone. The condition is without grave significance as far as the heart is concerned. Occasionally a toxic condition affects the sinus node or there may be some condition affecting the central origin of the vagus. Frequently these patients suffer from syncope. Low blood-pressure is commonly found. If in such individuals this type of an irregularity is observed, organic heart disease is sometimes erroneously diagnosed with much harm, and invalidism results from such an opinion.

Premature beats or extra-systoles, as they are frequently called, occur as an expression of increased irritability of the heart-muscle and thereby disturb the normal rhythm of the heart. These ectopic beats may arise from the auricle, the junctional tissue, or the ventricles. Those from the auricle and ventricle are more frequently encountered. Premature beats have been produced experimentally by electrical stimulation, by chloroform, asphyxia, and from various drugs, *i.e.*, morphine, caffeine, adrenalin, digitalis and strophanthin. They are frequently found in patients suffering from Graves's disease, and occasionally occur during infections such as typhoid, pneumonia, scarlet fever, diphtheria and from pyogenic organisms. There is a large group of valvular and degenerative heart disease patients, in whom premature beats are found. A small group of gastro-intestinal cases are associated with them. The affections of

the gall-bladder are more likely to be accompanied with premature beats than any other disease of the gastro-intestinal tract. Intoxication from tobacco, alcohol, coffee and tea, may also be associated with them. Another group, larger than any of the others, is frequently seen. In this group no other evidence of heart disease, or any organic disease, is discovered.

When considering statistics, it is important to analyze their source. For example, if one reads the statistics from heart clinics to which a large number of crippled cardiac patients come, then the percentage of associated heart lesions with premature beats would be large. On the other hand, if one reflects upon his own everyday experience in all medical cases, he will find a very large group of patients with premature beats in whom no demonstrable cardiac disease is present. Possibly because of the difficulty of diagnosis in the early recognition of heart disease, these signs are misinterpreted. Perhaps they are the earliest signs of myocardial disease.

Premature beats have been found in infants. They are frequent in elderly patients, and are more commonly found in men than in women. The associated lesions determine the seriousness of premature beats. Frequent premature beats add a strain to the heart by occurring before the diastole is completed, with the result that the output of the heart is thereby diminished. It is generally accepted that premature auricular beats, auricular flutter, and fibrillation, may be an expression of various degrees of increased irritability of the auricle. If one accepts this view, then the position of premature beats is a very important one in the management of the patient. A study of the electrocardiogram of ventricular premature beats will reveal a compensatory pause of such a length as to make a cycle equal to two cycles of normal rhythm. In those of auricular origin, the corresponding pause is less, so that the entire cycle is less than two regular beats. At times the patient is not conscious of premature beats, while at other times, he feels a sensation of fainting and a distinct thump, which in most cases causes him to consult a physician. Certain observations are helpful in detecting this form of arrhythmia. Attention to the pulse will reveal a feeble or absent impulse. On examination over the mitral area, we will hear an irregularity in which the first sound is heard, while the second sound is lost and three sounds will be heard instead of four. If the rate

of the heart is increased they usually disappear unless there is an extensive myocardial involvement. They become more pronounced when the heart slows. In several cases of premature auricular and ventricular beats, I heard them more markedly when the patient was in the prone position. During fever or intoxication they may appear and indicate an involvement of the myocardium. When a patient is under digitalis therapy, their appearance indicates evidence of toxicity from the drug.

In discussing tachycardia, it is important to recognize that there are two distinct types of tachycardia; one is the so-called "physiological" type in which responses occur to fevers, exercise, and intoxications affecting the sino-auricular node or vagus control; and the other is the pathological paroxysmal tachycardia. In this latter condition, there is evidence to warrant the statement that there is damage of the myocardium. The occurrence before the paroxysm of premature beats which have the same characteristics as the onset of the paroxysm, strengthens the belief that they have a common site of origin. The relationship between premature beats, paroxysmal tachycardia and flutter, is very close. I now have a patient in whom I have seen at various times these different types of disturbances.

The idea of circus movement around a separate focus has been offered as an explanation of the mechanism of paroxysmal tachycardia. There are cases associated with emotional states as well as with gastro-intestinal conditions. One patient, I observed, continued to have recurrent attacks until she was treated for gastric ulcer. This brought about a complete cessation of the tachycardia. The rate is usually 180 to 200 over the apex, and the heart-sounds are of a tic-tac quality. If a murmur has been present previously, it may disappear during the paroxysm. This is important to bear in mind in correlating the evidence when a patient is first observed during the height of a paroxysm. Various distressing symptoms, such as nervousness, exhaustion, fatigue, flatulence, and vomiting, may appear. Signs of cardiac failure, evidenced by an enlarged, engorged liver, moist râles at the bases, and œdema of the legs, may come on rapidly. The attack of tachycardia and these signs may first appear during an operation with serious consequences.

The important points in the recognition of this condition are:

- (1) The age of the patient (usually in a young adult or middle age

individual); (2) the history of an abrupt onset and a sudden cessation; (3) the persistence of the tachycardia regardless of position; (4) the rate is very constant (repeated examination of the rate while the paroxysm is present will show a very remarkable constancy); (5) the effect of vagus stimulation should be observed.

The tachycardia may be of ventricular origin showing, as its distinguishing features, a variation in the pauses between beats. It is not affected by vagus stimulation, while that of auricular origin may or may not be affected.

Auricular flutter is a type of arrhythmia characterized by rapid heart action. It has been observed in infants and young people but occurs chiefly in elderly patients. It may be transient or it may persist for many months. The condition, therefore, may be acute or chronic. It is probably dependent upon pathological changes in the auricle, such as a fibrosis or an interstitial myocarditis. This myocardial change may result from arteriosclerotic changes, valvular disease, or may be due to some acute infection, *e.g.*, diphtheria, rheumatic fever, scarlet fever, pneumonia, or syphilis. There is assumed to be present within the auricle, an area of increased irritability. Normally the impulse travels through the auricle to the periphera, radiating in all directions until it reaches the end of its path. However, in auricular flutter it has been found that there is present one contraction wave which constantly passes around a circle between the superior and inferior vena cava, having a definite time limit and a refractory period so that when the wave returns to its starting-point the place is receptive for it. This conception of the mechanism of auricular flutter is called the circus movement. The rate of passing over the circular mass determines the rate of auricular contraction. The auricles may beat from 260 to 350 times a minute. The ventricles usually respond to half of the impulses so that there is a 2 to 1 block. However, there may be present a 4 to 1 block with the ventricular rate of 75. Once established, this rate is remarkable for its constancy while the attack is on. It is not influenced by exercise, stimulation, or posture; but may be influenced by vagus pressure and digitalis. One observer noted a heart-rate of 140 over a period of seven years, which was due to this condition.

Auricular flutter is more frequent in males than females. It does not cause as much discomfort as the paroxysmal tachycardia

with which it may be confused. There is usually a history of repeated attacks of palpitation until finally one attack persists, leaving the heart constantly rapid. If such a history is obtained, particularly in an elderly patient in whom the apical rate is 130 or more, flutter should be suspected. Paroxysmal tachycardias, with which this may be confused, usually have a higher rate and a history of an abrupt onset and sudden cessation. Exhaustion and fatigue are accompanying symptoms, while signs of cardiac failure are rare.

It is important to discuss auricular fibrillation. Lewis states that it is responsible for 50 per cent. of the irregularities of the pulse which are encountered and that from 60 to 70 per cent. of the cases of cardiac failure admitted to the hospital manifest this disorder of the heart. The recognition of auricular fibrillation as a clinical entity is an excellent example of the value of animal experimentation and the use of graphic methods of study in the interpretation of the associated phenomena of the condition. In this way the proper significance of perpetual irregularity of the pulse and *delirium cordis* is appreciated. This is important because the condition affords the opportunity for the application of definite therapeutic agents whose effects are striking and at times dramatic and specific.

A brief review of the various conceptions of the condition is desirable so that it may be better appreciated as it is accepted and understood to-day. As early as 1850 Hoffa and Ludwig produced fibrillation of the heart-muscle by electrical stimulation. At first investigations were directed along separate channels—one, that of the arterial pulse—another, the study of the venous pulsation, and then later by means of electrocardiograms, resulting in a common conclusion. The irregular pulse associated with mitral disease, as well as the systolic pulsation of the veins of the neck, was studied by instrumental means. However, it was not until 1902 that correlation of the two phenomena was made. For this, credit is due to Mackenzie, who demonstrated their frequent association. He considered them to be due to paralysis of the auricle. Later, in 1904–1905, he changed his views that the auricle was in this state, because he had observed in these cases hypertrophy of the auricles at autopsies and also because he had seen cases restored to a normal rhythm. He reasoned from these observations that the auricle was in an active state. It is due to the efforts of Mackenzie that the condition slowly

came to be recognized as a distinct clinical entity. At first he felt that this condition following auricular distention was due to impairment of the junctional tissues, and in 1907 he offered the hypothesis of the possibility of its being of nodal origin and that the disturbance was in the auriculo-ventricular node. This view was later proven to be incorrect.

By producing this condition of the auricle in animals, various studies as to the nature of fibrillation were made. It was found easy to induce fibrillation of the auricle in dogs; and it was observed that while the auricles were fibrillating, there occurred a disturbance of the rhythmic contraction of the ventricles.

Cushny, in 1899, called attention to the similarity of the arterial curves obtained, in animals, by experimental production, of fibrillation of the auricles and those obtained from a case of paroxysmal irregularity of the heart in the human. Particular attention was called to the lack of relationship between the heights of the arterial pulses and the pause which preceded them. Fredericq was the first to record experimental evidence of the change in the venous curve of a dog, in a case of induced fibrillation. Comparison of the venous curves obtained from man in a case of complete irregularity of the heart and experimental fibrillation reveals similar curves. The absence of the "A" wave and the presence of tall waves in the venous tracing, together with rapid undulation of the veins of the neck when the heart beats slowly, are very important points to remember in the consideration of the various clinical phenomena obtained by bedside observation. Fredericq, in 1904, produced experimental proof of the relationship of auricular fibrillation and ventricular irregularity by cutting the bundle of His, following which the ventricles beat regularly. He then concluded that the ventricles had been beating irregularly in response to the fibrillating auricles.

Einthoven, in 1906, published the first electrocardiogram of clinical fibrillation. Herring, in 1908, Rothenberger, Winterberg and Lewis, in 1909, soon reported cases of fibrillation studied with the electrocardiograph. Among the first in America to use this method were James and Williams. This method of study soon created great interest in a problem which had been considered solely one for the physiologists.

The electrocardiograms, in cases of perpetual irregularity, re-

vealed the absence of the normal "P" waves, absolute irregularity of the ventricle, with no relationship between the height of the "R" wave and the preceding pause, and the presence of "F" waves. All of these conditions are not present in the other forms of irregularity of the heart. It was then assumed that the trouble was in the auricle and that there was a disturbance of the electrical potential of a distinctive and peculiar nature. The auricle was considered active because of the peculiar oscillations observed throughout the cardiac cycle. These oscillations were considered an essential feature of complete irregularity of the heart. The final proof of this is the comparison of observations made on man and animals. This was done by Lewis. He observed six horses with complete irregularity of the heart. He obtained arterial and venous tracings and electrocardiograms of the same character as those from man. One of the animals was thrown and shot through the brain, the chest quickly opened, the ventricles were seen to be beating rapidly and irregularly. Lewis's statement follows: "At first no intrinsic movement could be seen in the auricle. Its walls seemed fixed in diastole but close inspection revealed fine fibrillary movements. Thus comes the final and ocular proof that experimental fibrillation, as we know it, occurs as a manifestation of disease."

Various theories have been advanced concerning the nature of fibrillation. Increased irritability was considered to be a cause. Engelman, in 1895, advanced the idea that in fibrillation the muscle-fibres contract independently. Winterberg claimed that because of increased irritability there were present multiple foci of impulse formation. For many years Lewis was a strong advocate of this view, only to abandon it later in favor of the circus movement as suggested by Garry and Mines. Mines described this movement as a wave of contraction which passed around a ring so that there was a refractory period of such length as to allow it to pass as the crest of the wave approached it.

It had been previously demonstrated by Garry that definite blocks of auricle could be clamped off and that contraction would occur in the blocked-off portion. He later suggested that there were present in fibrillation, varying differences of excitability and conduction, causing to be present varying degrees of block due to change in the refractory state of the muscle. He states that, "Im-

pulses can spend in any and all directions, their progress being limited only by the pre-existence or development of localized blocks within the tissue mass. Such blocks divert the impulse into other and more circuitous paths, and the area so blocked can participate in contraction only when an impulse which has passed the other part of the ventricle approaches it from another direction. The area in turn becomes a centre from which the progress of contraction is continued, to be in turn diverted by other blocks."

The existence of such blocks, and especially blocks of transitory character and shifting location, has been noted. These conditions make possible the propagation of the contraction wave in a series of ring-like circuits of shifting location and multiple complexity. It is in these circus contractions, determined by the presence of blocks, that we see the essential phenomena of fibrillation. The use of the term "circus movement" has been continued since. The various leaders have accepted the explanation as offered in the circus movement theory as the most logical one for the mechanism of fibrillation. Varying degrees of conduction period, refractory state of the muscle, and the length of the wave, have been considered essential. Lewis and his co-workers have confirmed the circus movement theory by experimental work. By means of digitalis, atropine, and quinidine, they have attempted to explain some of the problems and conditions of fibrillation and their relationship to the circus movement theory.

The evidence is strongly in favor of the theory; and since it has been accepted, the condition of flutter is considered as closely allied to fibrillation, the difference being the length of the gap between the crest of the wave and the refractory state of the muscle. These factors determine whether there shall be a regular auricular contraction following a circular path, or contractions which are constantly irregular and with varying paths followed by the contraction wave. Lewis has shown that the circus contraction occurs in a ring of auricular muscle around the superior and inferior vena cava.

Fibrillation of the auricles may be transient or permanent. In the transient form there is obtained in the history, recurring and distressing palpitation. This type often leads to the final permanent stage. Krumbhaar reports several instances of transient fibrillation which were observed in the following conditions: During the course of a pneumonia, in a highly neurotic woman who had a syphilitic

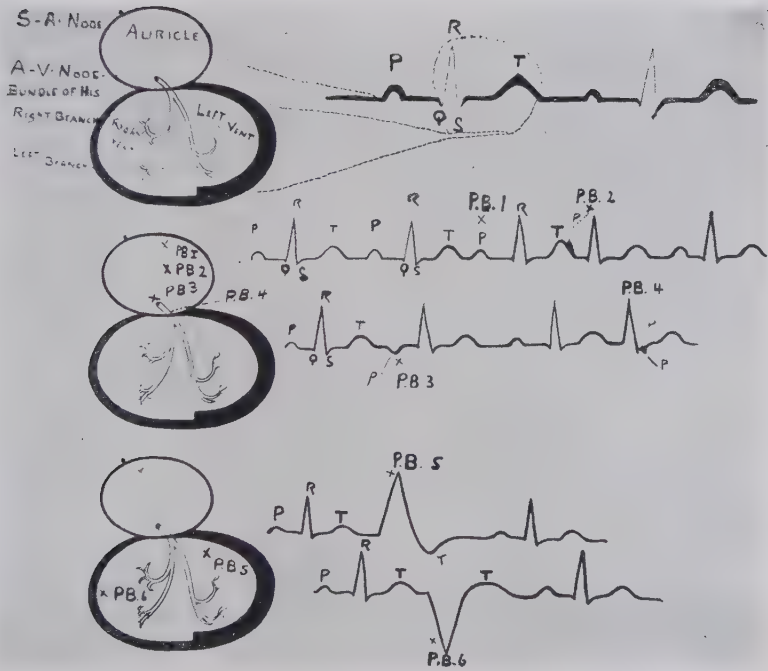
myocarditis, and in a man who was suffering from myocarditis. Cohn has repeatedly observed it during the study of pneumonia. It has also been observed in a healthy man following hydrogen sulphide poisoning. F. Smith produced transient fibrillation of the auricles by deep breathing. There is a possibility that this condition is a more frequent one than is realized.

The onset of fibrillation may be insidious and without warning. In fact, it may be accidentally discovered that the patient has an irregular pulse. It may be the only evidence of cardiac disorder or it may be associated with other severe cardiac involvement. Complete arrhythmia may be present with various degrees of cardiac embarrassment, *e.g.*, dyspnoea on exertion, to the more pronounced symptoms of decompensation.

It is important to recognize the two essential conditions of complete arrhythmia, namely, the fibrillation of the auricles, and the irregularity of the ventricles. Particular stress should be laid upon the condition of the ventricles since proper appreciation of it will materially influence the treatment and prognosis. The integrity of the heart-muscle is the key to the situation. A rapid, irregularly acting ventricle is headed toward disaster with serious consequences unless the rate and the rest period of the heart are controlled. There is a possible danger in the term "auricular fibrillation" if it conveys to the mind only the disturbance of the auricle.

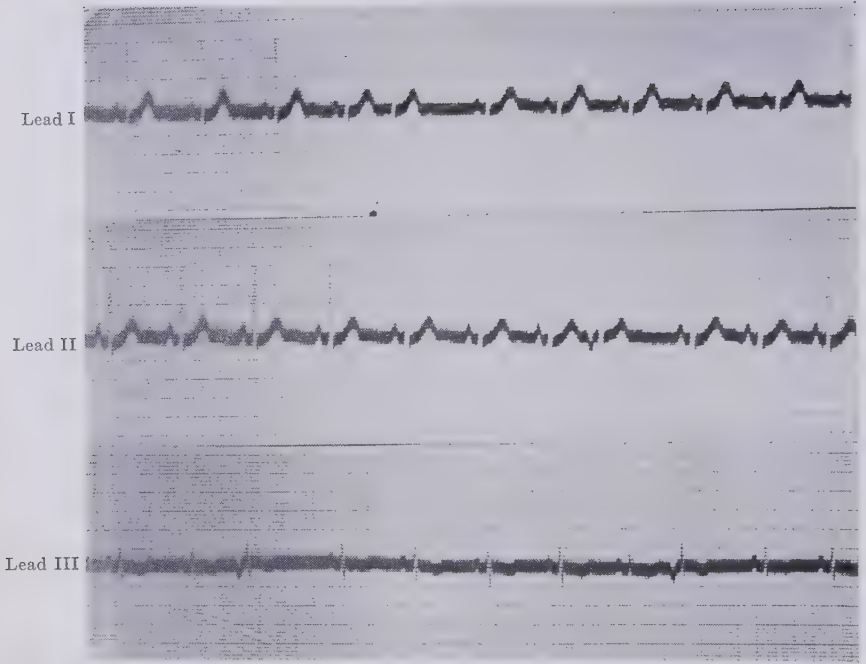
The condition is rare in children even in the presence of valvular lesions. Inasmuch as fully 50 per cent. of the cases observed are associated with mitral lesions, it is more frequently found between the third and fourth decades. There is, however, a large group of cases, particularly in males, which are observed between the fifth and sixth decades. This is in the group where myocardial degeneration is present. There are instances, however, in this group, where there is no evidence of myocardial weakness, the only abnormal finding being the arrhythmia. In view of the general prevalent idea of the relationship of auricular fibrillation to rheumatism and mitral disease, it is important that particular attention be directed to this latter group. Levine has stated that organic mitral disease is rare in an individual over fifty years of age. This is important to consider in view of the frequency with which mitral murmurs are heard in these patients. He further states from the study of 126 consecutive cases

FIG. 1.



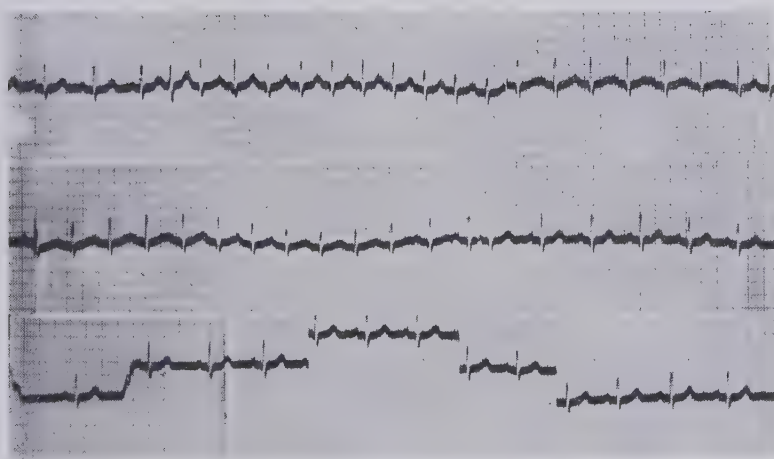
Schematic diagram to illustrate the location of the S.-A. Node; the A.-V. Node; the bundle of His with the right and left branches; as well as the possible site of impulse formation of various premature beats. (Modified from a diagram by Dr. S. A. Levine in the Oxford Loose Leaf Medicine.)

FIG. 2.



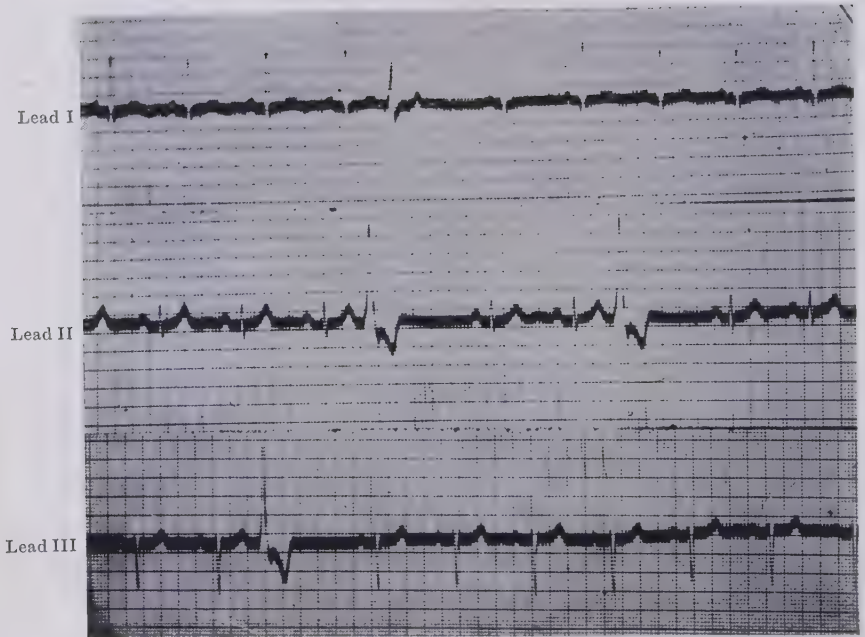
Premature auricular beats showing inverted P. in leads II and III.

FIG. 3.



Auricular tachycardia, lead I.

FIG. 4.



Premature ventricular beats.

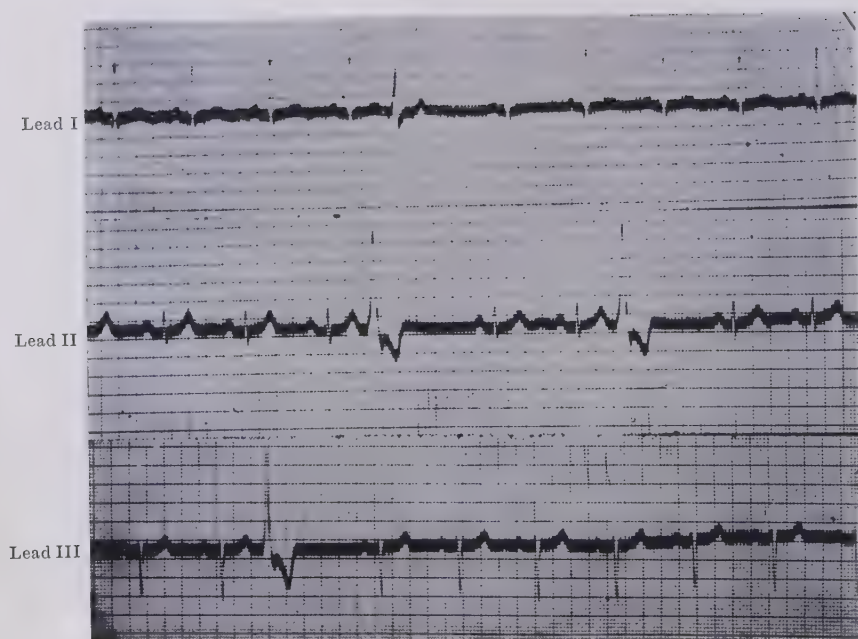
of auricular fibrillation, that it is almost as common in hospital practice as lobar pneumonia. Lewis states that 60 to 70 per cent. of cases admitted to hospital with cardiac failure have auricular fibrillation. It may occur during acute infections, especially pneumonia.

While rheumatism is considered the predominant etiological factor, it is frequently found to be associated with thyrotoxic hearts and may occur during or after a surgical operation. Many of the arrhythmias which follow anæsthesia and operations are of this type. Drugs, nervous strain, emotions, adrenalin and iodine, have all produced it. In many instances myocardial changes are found, such as subacute and chronic inflammatory conditions progressing to fibrotic changes, but because the microscope does show these changes, it does not prove that they are the cause of the disturbed function of the auricle.

It is important to analyze the electrocardiograms obtained from typical cases of auricular fibrillation. By so doing, one will be able to find an explanation for the many signs observed in the condition, which later should enable one to diagnose the condition without graphic study. The first observation is the definite irregularity of the ventricular complexes. The "R" deflections do not occur regularly. Their height bears no relation to the preceding pause. The absence of "P" waves is noted, and there is observed, sometimes, only a slight oscillation of the string. At other times, rapid, coarse oscillations are seen. The entire picture is one of irregularity in form, amplitude, and frequency. If, to this picture given by the electrocardiogram, one will add the evidence obtained by the graphic study of the venous pulse, then a sound explanation of the signs observed will be found. With this information before us, these signs will be more easily detected and appreciated by the usual physical examination.

Let us consider first the evidence obtained by inspection. If one will carefully examine the supraclavicular spaces and note the condition of the veins, especially at the end of a forced expiration, he will be surprised to note coarse or fine undulations. The coarse waves will be evident. The fine waves will have to be carefully looked for. Upon palpation much information is obtained. The finger over the radial artery will detect an irregularity in the force of the beats. If one will count the radial pulse for at least two minutes instead of the usual custom of one-quarter minute, one will be im-

FIG. 4.



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pressed, not only with the change in the force of the beat, but also in the rate of the beat for every five seconds of the period. Some beats will be scarcely felt. This becomes more evident the faster the heart is beating.

The slow ventricular rate is one in which fibrillation may not be thought of, as is also the case with the rapid regular ventricular rate in which a careful study of the radial pulse and veins of the neck is necessary. Exercise will make the irregularity more manifest. The examination of the apical rate with the stethoscope will soon disclose an evident irregularity of the heart, characterized by irregularity in force, rhythm and rate. The relationship between a long pause and the following beat is such that there is no renewed strength to the beat. The rate will be found higher than the radial pulse; that is, there is present a pulse deficit to which attention was called by Draper. When the blood-pressure is taken, it is observed that certain beats fail to reach the bend of the elbow and are not heard. The cuff is deflated to a lower level and a few more beats are heard. This is continued until, at a much lower level, more of the beats appear to come through. Because of this, blood-pressure readings are unreliable unless one uses the method that was suggested by James and Hart.

Careful correlation of the above evidence, with the observation of the effect of exercise, will enable one to recognize at least 90 per cent. of the cases of fibrillation. Difficulty may be encountered in those cases where there is a slow ventricular rate. Similarly, fibrillation may not be thought of in a fast, regularly beating heart. Here, however, helpful aid may come from careful inspection of the neck. A careful prolonged study of the radial and apical rates and the effect of exercise is necessary since the faster the heart beats, the more evident becomes the irregularity. This fact assumes greater importance if the rate is over 120 per minute.

Heart-block is another type of arrhythmia occasionally met with in practice. Fortunately, it is rather uncommon. Heart-block may be acute, or chronic; it may be partial, incomplete, or complete. The lesion is usually in the bundle of His, and there is an interference with the conduction of the impulse from the "A-V" node to the ventricle. Heart-block occurs during infections, especially rheumatic fever, scarlet fever, pneumonia, typhoid, and pyogenic infec-

tions. It may be unmasked by digitalis. Chronic heart-block is due to definite pathological changes in the bundle of His. Usually this is just an expression of widespread myocardial changes. Rheumatic fever and syphilis are the common causes.

The earliest stage of block can only be recognized with certainty by instrumental means; however, when this persists for some time, there is found evidence of increase in the block, characterized by dropped beats. Digitalis may cause them to appear, and it is now generally agreed that when drop beats do occur under digitalis, that there must have been present a change of the bundle which was aggravated by the digitalis. Dropped beats may occur every 10th, 9th, 8th, 7th, 6th, 5th, 4th, 3rd or 2nd beat. They may be confused with premature beats but should cause no difficulty if one pays careful attention to auscultation over the mitral area, for one will easily note the missed beats by the characteristic change in the rhythm. Furthermore, if in doubt one should try vagus pressure. This will cause more dropped beats to occur if heart-block is present. When heart-block is complete, it can be recognized by clinical methods. The low ventricular rate of thirty to thirty-five is important. The changing intensity of the sounds over the mitral area is noted and is an important observation.

In view of the possibility of digitalis unmasking a previous lesion of the bundle, caution in its administration is necessary. When dropped beats are heard, it should be avoided. Similarly, during an acute infection in an elderly patient, the sclerotic changes previously present are made manifest by the toxic effect of the infection upon the bundle; and dropped beats appear more frequently, thus indicating an involvement of the myocardium; but it does not indicate the administration of digitalis. Extreme caution in its use should be observed.

Recently I examined two elderly patients in whom this experience occurred. One had a phlebitis of the leg and an infected bladder. Dropped beats occurred at the rate of seven per minute. No digitalis was given. Treatment directed to his phlebitis and bladder enabled him to recover, so that now no evidence of dropped beats is found. The electrocardiogram does not reveal any heart-block at present. Another man, suffering from severe myocardial disease with changes of a degenerative type, developed occasional dropped beats. He was

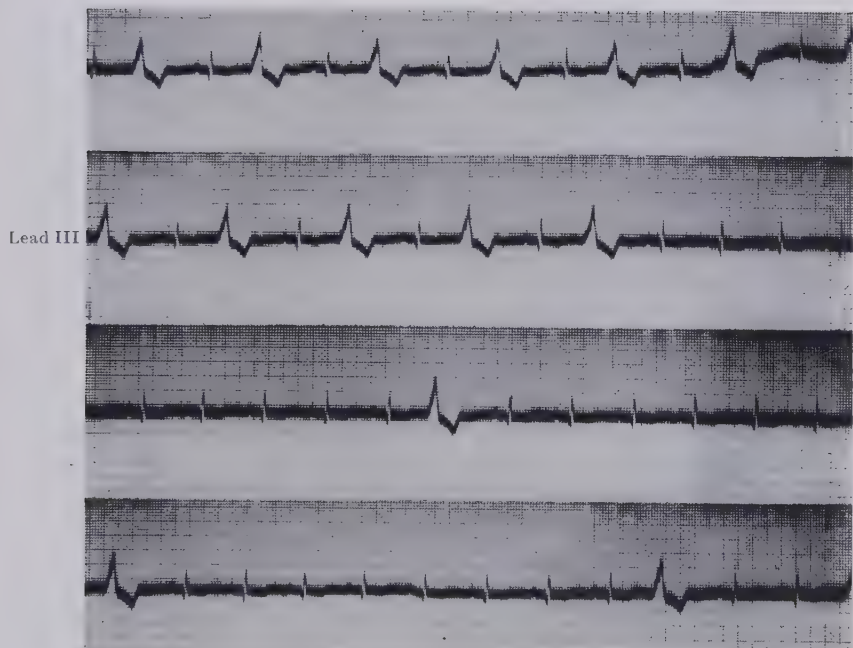
receiving, at the time, small doses of digitalis; vagus pressure increased the frequency of the dropped beats and when digitalis was discontinued, the drop beats disappeared. It is very important to recognize that some patients are susceptible to digitalis. This susceptibility may be related to changes in the conducting system so that various forms of heart-block are easily produced even with small doses of digitalis.

TREATMENT

The Treatment of Sinus Arrhythmia.—There is no therapy for it. Digitalis is contra-indicated. Greater still than the importance of its recognition is the fact that if undue emphasis be put on this simple arrhythmia, a permanent cardiac invalid may be produced. Simple tests of exercise, breathing, and the administration of belladonna will aid in clearing up an arrhythmia of this type. For this condition there is no need of enforced rest or cardiac remedies.

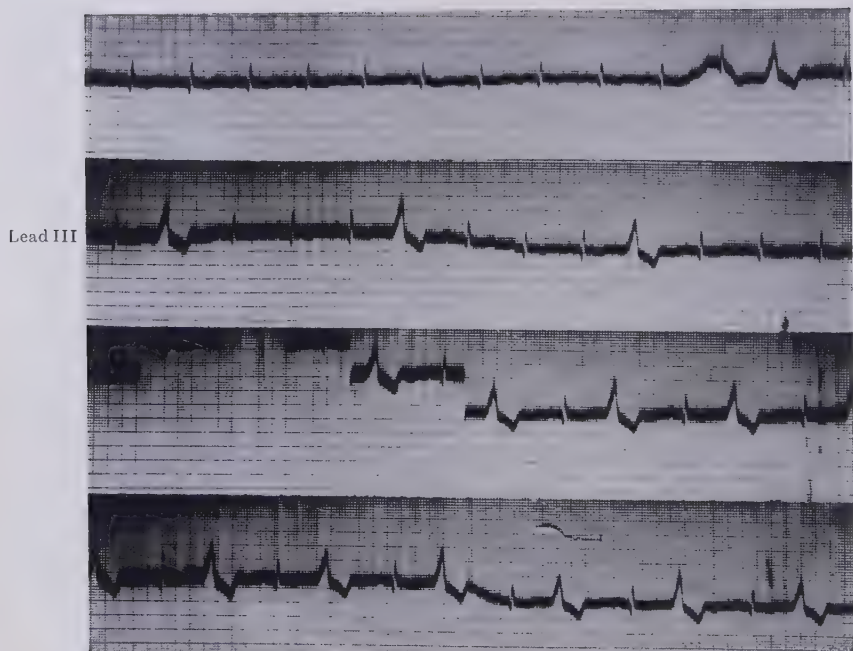
The Treatment of Premature Beats.—This condition requires a careful study of possible etiological factors. The heart must be studied for other evidence of disease. Various foci of infection must be searched for, and careful inquiry must be made for possible intoxication from drugs, especially digitalis previously given, because a murmur or an irregularity had been detected. The habits of the patient should be carefully inquired into, particularly as to the amount of coffee, tea, alcohol, tobacco, and sweets used. The gastrointestinal tract should be carefully studied. Sometimes, however, one is left with premature beats as the only physical finding. Reassurance that there is no organic heart disease is all that is frequently necessary. There are instances, however, where these premature beats occur so frequently and cause such uncomfortable sensations that medication is desirable. Various drugs have proven helpful. In that type of very nervous women, especially during the climateric where at times hypertension is noted, and the blood-pressure is found to be unstable, along with other signs of instability of the nervous and vascular systems, the bromides and other sedatives have served me well. The use of quinine and some of its derivatives has been very helpful in allaying the distressing symptoms. Strychnine added to quinine has also been helpful. Sometimes measures to increase the heart-rate are helpful. Belladonna may then be used.

FIG. 5.



Continuous lead. Premature ventricular beats showing interpolated beats. This patient had not received any digitalis.

FIG. 6.



Continuous lead. Premature ventricular beats showing interpolated beats. This patient had not received any digitalis.

In view of the occurrence of premature beats under digitalis therapy, we should not prescribe it for this arrhythmia, unless there is other evidence of myocardial disease. Likewise, the activities of the patient should not be restricted because of this form of arrhythmia, unless associated with other evidence of myocardial disease.

The Treatment of Paroxysmal Tachycardia.—There have been numerous remedies and suggestions offered for the management of these cases. The patients frequently use measures of relief such as the induction of vomiting, the drinking of hot or cold water, attempts at swallowing, and deep breathing. All of these have a vagus effect and are frequently effectual. There are times when one measure will succeed and the next time it will fail. An attempt to break up the attack should be made by trying the effect of vagus or ocular pressure. Digitalis given so as to keep the patient completely digitalized is sometimes of service. With the conception of increased irritability of the auricle or ventricle, quinidine may be used to lessen the irritability.

In estimating the value of any of these procedures, it is always important to keep in mind the fact that these paroxysms frequently have an abrupt termination. The frequency, duration, and the gravity of the attack, together with the condition of the heart-muscle and signs of failure, determine what course to pursue.

The Treatment of Auricular Flutter.—For transient attacks, quinidine treatment is usually successful. If the attack has been present for some time, then digitalis should be given. The method of giving digitalis is important. It should be given in full doses to obtain a definite slowing of the ventricles; then this slowing should be maintained, and finally the dose increased so that fibrillation is produced. When one reaches this point, if the remedy is now withdrawn, the fibrillation will cease and normal rhythm return. The secret of success is in trying to block the circus movement of the auricle.

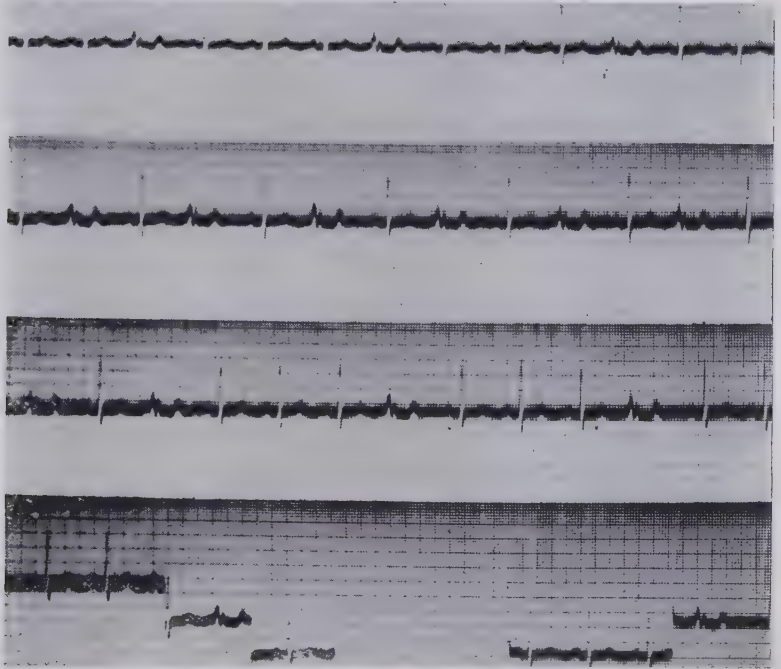
The Treatment of Auricular Fibrillation.—A thorough understanding of the mechanism of fibrillation, the conditions under which it may arise, and an appraisal of the associated lesions, determine treatment. Each case must be carefully studied. Thyrotoxicosis is a frequent cause of auricular fibrillation. Proper treatment of this condition by means of rest and surgery, with proper medication for

the heart, has restored many cases of this type to normal rhythm. When auricular fibrillation is the only evidence of cardiac disorder, quinidine has proven extremely valuable. The successful return to normal rhythm is more certain if fibrillation has not been present very long. Quinidine certainly occupies a place in the treatment of this condition. Patients should be previously treated with digitalis. Experience teaches us that even if the rhythm is not restored, the patients, subjectively, seem better. The presence of congestive failure, advanced mitral disease, or if the fibrillation has been present a long time, contra-indicates its use. Furthermore, it should not be used unless it is carefully followed with electrocardiographic studies.

There are possible dangers in its use. In practice then, the main remedy is digitalis. It has been and is now the chief remedy in the treatment of fibrillation. Digitalis does not remove the fibrillation of the auricle but does influence the effect of the fibrillating auricle on the ventricle. The presence of fibrillation itself does not warrant the use of digitalis. Each case of fibrillation should be studied individually. The rapid heart action shortens the rest period; and this with improper filling of the ventricles favors myocardial weakness. Digitalis is given with the idea of blocking some of the impulses which come down from the auricle and thus enable the ventricle to have its proper diastole. In order to do this, digitalis should be given in such doses until the apical rate is between 70-80, and then enough digitalis given to maintain the rate. Each case must be worked out individually. The radial pulse is no guide; frequent failures occur from the sole dependence upon it as an indication of the heart-rate. Another source of failure is insufficient dosage. The following may be mentioned as possible explanations of failure in the treatment, with digitalis, of auricular fibrillation: (1) Inert digitalis preparations, (2) insufficient dose due to confusing drops with minims, (3) fear of over-dosage, (4) lack of familiarity with the effect desired from digitalis, (5) lack of familiarity with the toxic manifestations of digitalis. It should be the duty of each physician to find a potent digitalis preparation. He should clinically test the preparation himself, watching for certain effects, namely, slowing of the heart-rate, increased output of urine, and nausea. The very high-priced digitalis remedies are no more effective than a good potent standardized tincture, or powdered leaves. In my experience,

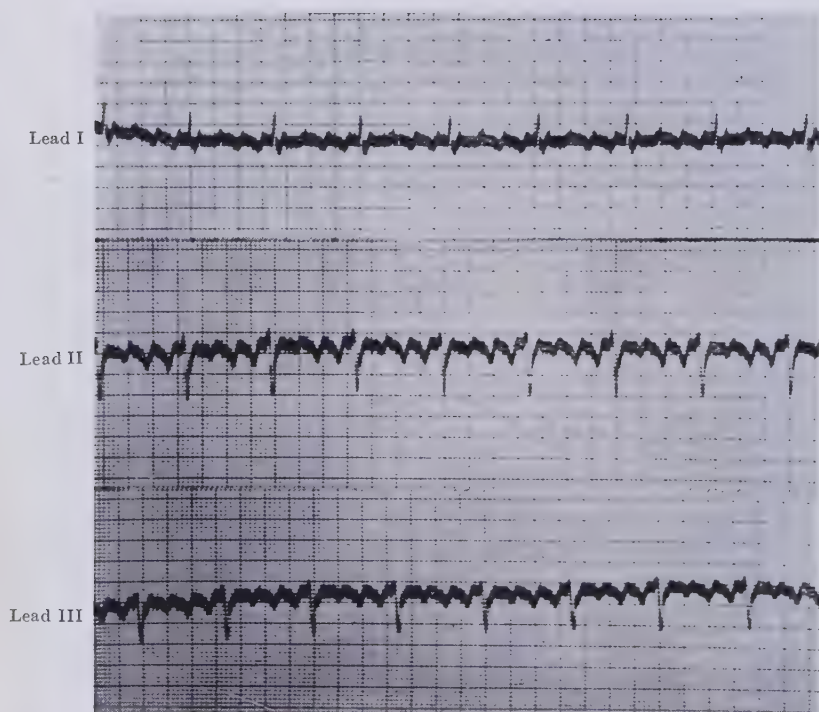
FIG. 7.

Lead I



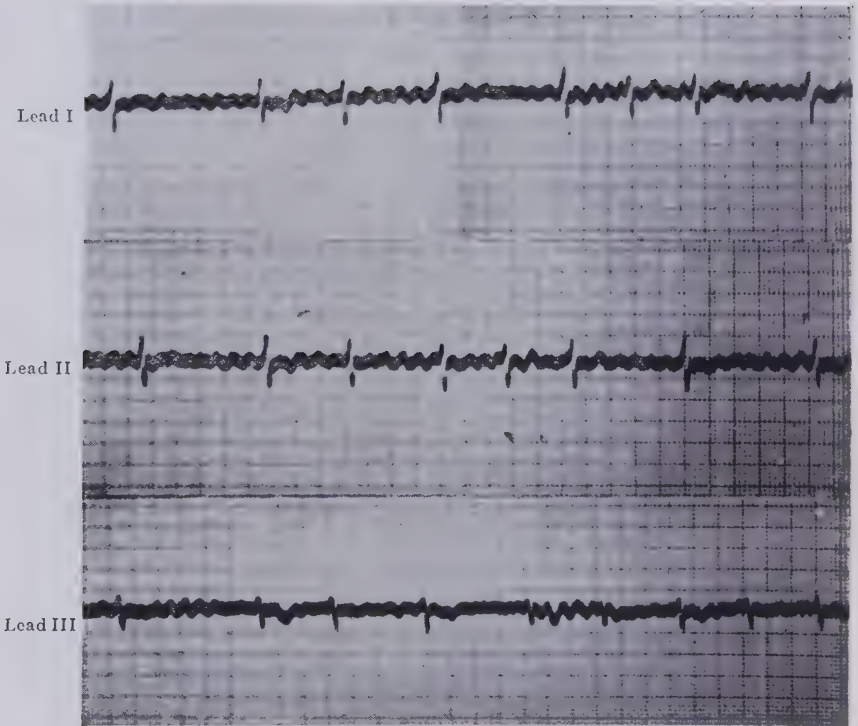
Continuous lead. Premature ventricular beats showing interpolated beats. This patient had not received any digitalis.

FIG. 8.



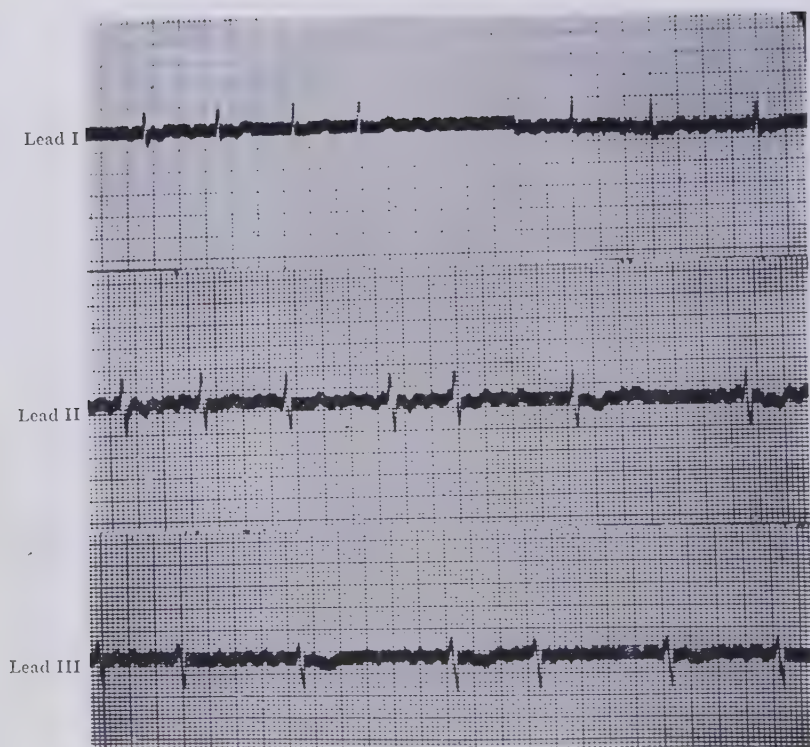
Auricular flutter. Note the regularity of the auricular contractions with a 4 to 1 block.

FIG. 9.



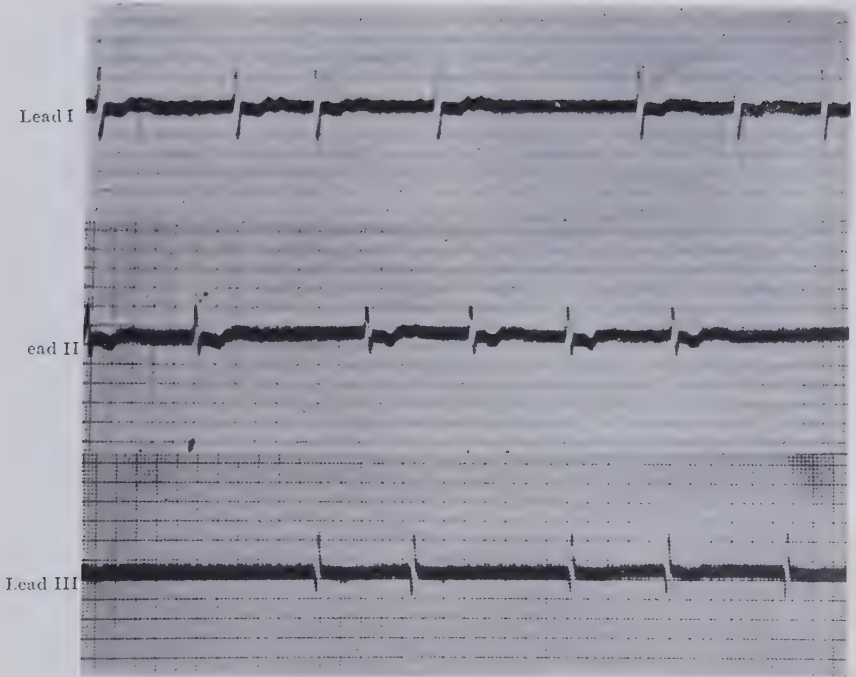
Auricular fibrillation. Note the absence of "P" waves, presence of "F" waves with irregular ventricular responses.

FIG. 10.



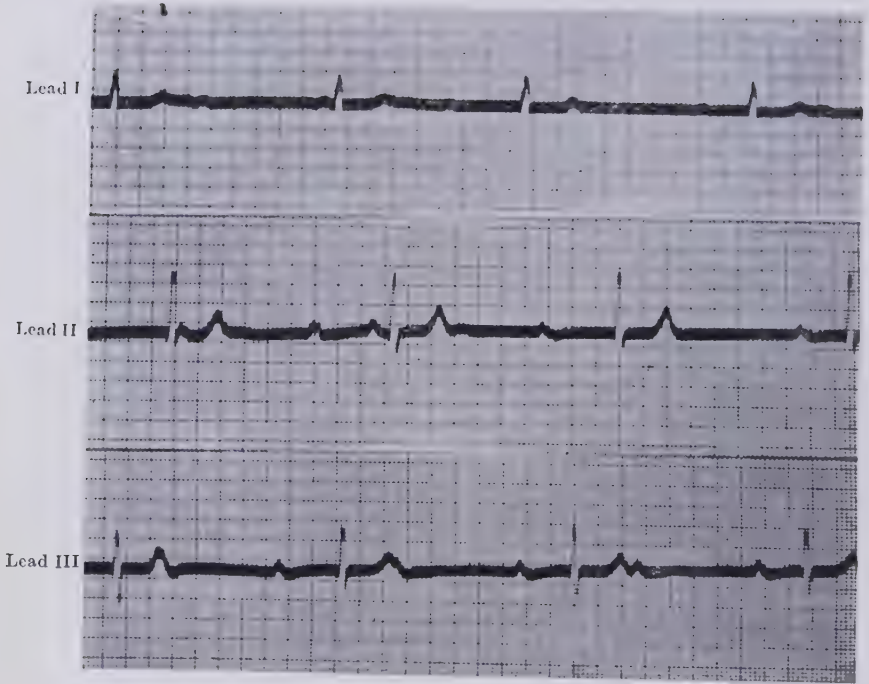
Auricular fibrillation. Note the absence of "P" waves, presence of "F" waves with irregular ventricular responses.

FIG. 11.



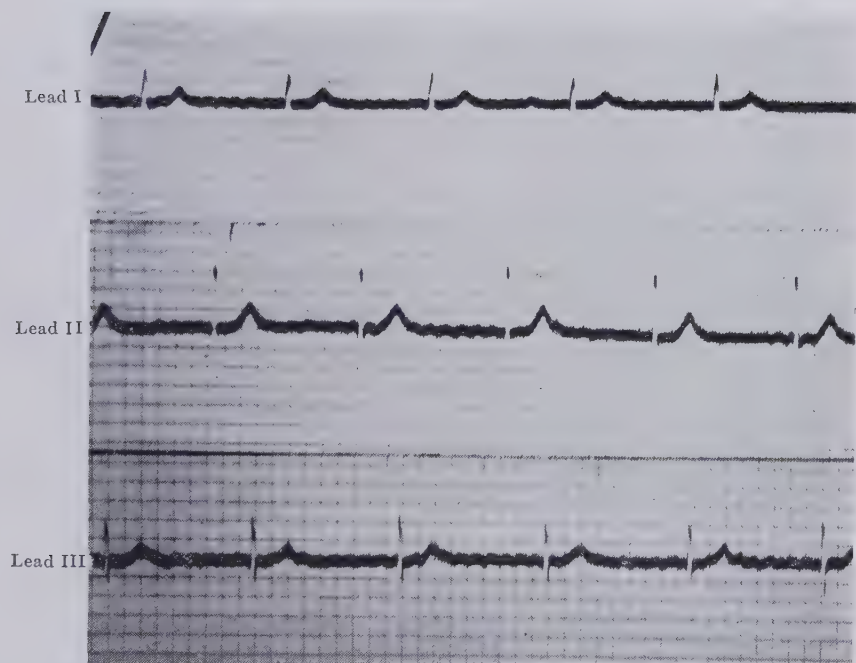
Auricular fibrillation after digitalization. Note the absence of "P" waves, presence of "F" waves with irregular ventricular responses.

FIG. 12.



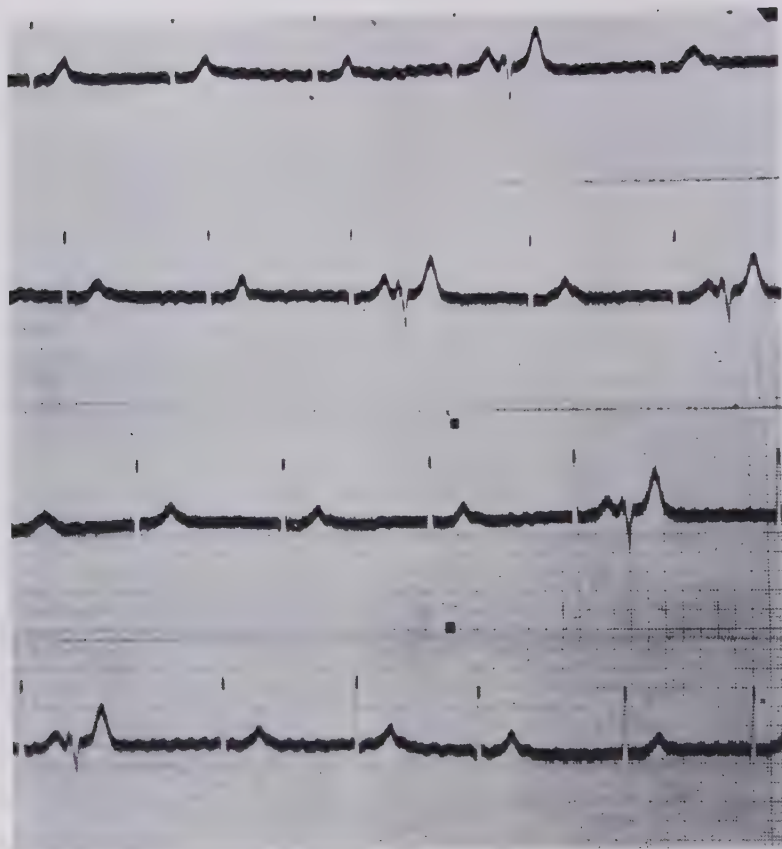
Heart-block. Complete disassociation of the auricle and ventricle.

FIG. 13.



Heart-block with auricular fibrillation. Note the absence of "P" waves, presence of "F" waves with regular ventricular complexes.

FIG. 14.



Lead II. Heart-block, auricular fibrillation and premature ventricular beats.

I have seen more harm come from not giving enough digitalis than too much. One of the commonest causes of this has been the dependence upon a medicine-dropper as indicating a minim.

It is difficult at times to detect a fibrillation when the heart is slow and normal rhythm is present, and caution is necessary in stating, upon this evidence, that the fibrillation has disappeared. The electrocardiogram shows the persistence of the fibrillation after the heart has been slowed by digitalis. Failure to appreciate this fact is responsible for many recurrences of myocardial failure because, after the heart has been slowed, the digitalis is discontinued and the patient allowed to drift along, only later to return with a more badly damaged heart.

Following the administration of digitalis, the heart is slow and apparently regular. Efforts to increase the rate may reveal an irregularity which was not previously suspected and a correct interruption of it as fibrillation will be definite indication for the continued administration of digitalis to maintain the normal heart-rate. When other evidence of heart disease is present, treatment should be directed for it.

The Treatment of Heart-block.—The treatment for heart-block demands careful attention. The age of the patient is helpful in determining whether there is a likelihood of permanent extensive damage of the bundle, or not. The presence of an infection of any kind, particularly syphilis, will determine treatment. One should use caution in the use of digitalis. Atropine has been used as a vagus depressant. In recent years, iodine and thyroid extract have also been used with some success. I recall one man whose ventricular rate was increased by thyroid extract and he was made very comfortable. Barium chloride has also been recommended.

Figs. 1-14 should be carefully studied as they will be found to elucidate the text on many important points.

SUMMARY

(1) In view of the frequency of cardiac irregularities, it is important that one be familiar with the mechanism of the impulse formation and its transmission through the heart.

(2) Many of these irregularities can be clinically recognized.

(3) The importance of: (1) A careful correlated history; (2)

the age of the patient; (3) respiration effects; (4) the effect of vagus pressure; (5) infections; and (6) exercise, are paramount.

(4) In view of the fact that under digitalis therapy, some of these irregularities appear, and then disappear when it is discontinued, this drug should only be given where there are definite indications for its use.

(5) Every effort should be made to recognize auricular fibrillation and differentiate it from other arrhythmias since it offers to physicians an opportunity of using digitalis in a definite and positive manner with benefit to the patient.

(6) That, while an arrhythmia may be present, the all-important consideration is the question of the integrity of the myocardium and the associated lesions; such as chronic valvular disease and hypertension, as well as reflex disturbances, intoxications and infections.

I wish to acknowledge my appreciation of the helpful suggestions made at various times by Drs. Samuel A. Levine, of Boston; Thomas McMillan, William Stroud and James E. Talley, of Philadelphia.

THE TREATMENT OF APPENDICITIS *

BASED ON A REPORT OF A THOUSAND CASES

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THE treatment of appendicitis is entitled to and usually receives vigorous discussion when mentioned even in parlor conversation in most communities. In a large proportion of cases the physician is called after treatment by home remedies and store-bought medicines have failed to give relief. Over this factor doctors have only indirect control through education of the people. As soon, however, as a patient with abdominal pain comes under the care of a doctor, the problems are ours. They concern the diagnosis, the immediate treatment, the need for operation, the treatment preliminary to operation, the technical methods of operative procedure, and last, but by no means least, the treatment following operation. There are many points of overlapping responsibility on the part of everyone who gives advice to an individual suffering with abdominal pain. Successful coöperation is best secured when the views of physicians and surgeons can be brought in accord on at least the problems of vital importance. The testimony of general impression of those experienced in the business exhibits more appeal if supported by critical analysis of facts found in detailed case records after they become cold.

Clinicians and human beings may not escape the habit of expressing with some positiveness their fixed beliefs. Progress comes more quickly if one's beliefs are not so firmly fixed that they cannot be changed. Clinical experience yields clinical wisdom only to the mind wide open to change of opinion.

The present report of one thousand consecutive cases operated upon personally extends back a sufficient number of years to include every death that has ever occurred in my practice, either from the disease or from the operation up to February, 1925. That there may be no question as to the nature of the cases here reported, only patients

* Presented in abstract to the Richmond Academy of Medicine in February, and to the Medical Society of Virginia in October, 1925.

definitely showing acute, advancing, stationary, or subsiding symptoms and signs are included.

Every case has been personally studied from the beginning to the end of treatment and a record kept. In addition to the detailed study of each case as it goes along, the records have at intervals been studied in smaller groups while the details were fresh in memory and with certain specific problems in mind. In conjunction with my own work I have, through the courtesy of other surgeons, taken opportunity to study many other hundreds of cases, more especially the complicated and serious ones and cases treated by different methods. And finally now the records, thoroughly cold, of a thousand consecutive cases are to be analyzed for whatever truth may be brought to light. The cases in this series have been operated upon at all times after onset, at all stages of pathology and in patients in all sorts of general condition; good, poor, and wretched; with and without complications; with and without preliminary preparation. Various operative procedures and different methods of treatment before and after operation have been employed and opportunities for comparison are easily found.

There were twenty-one deaths in the entire series of one thousand patients operated upon, a mortality of 2.1 per cent.

Of 830 clean cases there were four deaths (less than 0.5 per cent.); few complications and sequelæ, the patients being well and out of bed in from five to seven days. Of 170 drainage cases, including regional and spreading peritonitis, there were seventeen deaths (10 per cent.) and a considerable number of complications to be mentioned later.

Of the total thousand cases, 925 were youths and adults with seventeen deaths (1.8 per cent.); only seventy-five were children twelve years old and under; of the children twenty-five were clean cases; fifty required drainage; one clean case and three peritonitis cases in children died.

The most conspicuous difference in the disease in children and adults is that the disease is much less frequent and more difficult to diagnose in children and they are more violently purged before operation. With these facts we wonder not that two-thirds of the cases in children require drainage, but that as many as one-third of the cases do not have extensive peritonitis.

The mortality of twenty-one cases in the thousand (2.1 per cent.)

is small; 0.5 per cent. in clean cases is small; 10 per cent. in cases of peritonitis is small compared with the results of other surgeons. But let us not boast of small mortality for it is much higher than it ought to be and I make bold to assert that the time is here for us to believe that most of the deaths from appendicitis are preventable and that it is our duty to restudy the details, find and correct the mistakes we have made and learn how to conquer the mortality of this disease.

The classification of appendicitis is a problem of fundamental importance. My practice has always been to have two classifications; one for the patient and one for the disease. Patients may be sick acutely or chronically, severely or slightly, temporarily or permanently with appendicitis; the symptoms are fulminating, advancing, subsiding, recurring and so on, in terms limited only by one's vocabulary, descriptive of symptoms and clinical course. Such terms are altogether relative and so obviously dependent upon the point of view that the inexperienced clinician may easily be misled into embarrassing surprise when he sees a rotten appendix, with spreading peritonitis, in a stoical person with a bold smile, no fever, and slight leukocytosis, who has often had "similar attacks" before; or into disgusting chagrin when he sees a slightly thickened, perhaps strictured, almost normal appendix removed at midnight from a patient who is writhing in agony, tossing with belly-ache, cannot stand being touched, and in whose blood, leukocytes and "polys" are found in large numbers.

There are four distinct types of surgical pathology upon which treatment is based.

(1) Pure appendicitis. There are œdematous swelling, redness, and often fecal concretions, but no disease of the surrounding peritoneum; no adhesions and no pus. Appendices only kinked and strictured, but not red or purulent or containing fecal matter, are normal appendices and though removed routinely when operation is performed primarily upon other organs in this region, are not recorded as cases of appendicitis. We constantly meet reports of such appendices as these in statistical reports; and we must watch carefully that reports of low mortality are not greatly diluted with recoveries following removal of this type of undiseased appendix. The only reason I mention these in this report is that two deaths, following operation in this type of case, have occurred and all deaths must be reported.

(2) Appendicitis with local peritonitis. In these there is swelling, redness, œdema, and pus, often with spots of gangrene in the appendix and its peritoneal covering, and yellow effusion without odor in the cavity.

Both the above types are of the group of clean cases in which after appendectomy the wound is closed completely, there is no need of drainage.

(3) Appendicitis with regional peritonitis, with or without walled-off abscess. In these the appendix is always gangrenous, obviously ruptured and its contents spilled into the adjacent space surrounded by bowel and omentum. The pus has fecal odor. The peritonitis is confined to the iliac fossa. Omental, bowel and often abdominal wall and pelvic organ adhesions partially or completely wall off the pus in the right iliac fossa, the pelvis, the retrocæcal and subdiaphragmatic areas and sometimes bowel obstruction is demonstrable. Though the pathology in such cases is terrible, one must not be deceived by thinking peritonitis is general and must equally carefully guard against deceiving others by statistics including these as cases of general peritonitis.

There are two easily recognizable types of abscesses: (a) Those of small size adequately surrounded by bowel and omentum but in which there is no contact with the anterior parietal peritoneum of the abdominal wall; (b) those large abscesses completely walled off on all sides by omentum and bowel and so adequately adherent to the abdominal wall that in operating it is quite unnecessary to open at any place the peritoneal cavity.

(4) Diffuse widespreading peritonitis extending beyond the iliac fossa with few light adhesions, into the pelvis, often the left side, and occasionally as far as the sigmoid, and often on the right, up under the liver.

There is great difference on the part of surgeons in their conception of widespreading or general peritonitis and consequently a lack of reliability of statistical studies of these cases. One must guard against deceiving and being deceived by few deaths from large numbers of cases of this type of disease.

When in the presence of as much as a teacupful of pus free in the cavity, without protective adhesions, the patient in desperate

condition with widespread rigidity and progressive distention, the case may be classified as one of spreading peritonitis.

Over 80 per cent. of the patients in this series were clean cases, *i.e.*, all the pathology was removable; there was no occasion for drainage. This fact is of great significance. This incidence of clean and suppurating cases is no different in the first hundred as compared with the last hundred cases, during which time there has been much appeal for early operation and great increase in the number of hospitals and doctors operating.

Every surgeon has observed that over 75 per cent. of the total number of adults operated upon for appendicitis give a definite history of having been attended through previous acute attacks of appendicitis, the symptoms of which subsided either undiagnosed or were deliberately permitted to do so without treatment or with proper treatment or in spite of what we now think is bad treatment and show at operation positive evidence of long-standing pathology.

Abscesses cannot reasonably be expected often to disappear spontaneously, though some doctors think they have ruptured into the bowel. In two cases operated upon months after subsidence of clinical signs of appendiceal abscess treated by competent physicians, there were such widespread and dense adhesions and definite absence of a part of the appendix that we were compelled to believe that abscess had existed. We have recently seen exactly the same thing happen in a child treated through the whole course of the disease and subsequently operated upon. Occasionally one sees sinuses of the abdominal wall due to appendiceal abscess. Such observations as these argue not for medical treatment of appendicitis and not for postponing operation. They are mentioned as facts showing remarkable ability of patients to handle their own disease successfully if given the proper help, and to be remembered before announcing to the bereaved ones of patients who die following operation, that because the appendix had ruptured or pus was present, they would surely have died more quickly if they had not been operated upon.

Surgeons, of course, see very few people die without operation. Physicians could help in this study by reporting the cases they have seen die without operation. Personally, I think I have seen four deaths from appendicitis and peritonitis unrecognized, not operated upon and badly treated. It is no uncommon experience to find at

operation all types of appendicitis and peritonitis previously undiagnosed. The number of people who are buried with appendicitis is unknown. Undertakers could secure valuable information on this question.

Despite the large experience all doctors have with appendicitis there is still a high percentage of errors in *diagnosis*. Who has not removed or seen removed at an "emergency" operation in the nearest hospital a normal, kinked or slightly swollen appendix with nothing the matter with it from a healthy fellow, an emotional young woman, or a sick child; and what surgeon of great reputation and authority has not been embarrassed by the surprise of finding a rotten appendix and peritonitis after days of observation, much examination by many doctors under the group system and perhaps some treatment of a stoical patient with few symptoms and a cheerful disposition?

Much of the difficulty encountered in making the diagnosis within the first few hours of symptoms is incident to the fact that the patient has taken medicine or may have eaten something to which the pain is assigned. The point to be determined is whether the symptoms in the given case are due to disease, food, or medicine.

Diagnostic errors are in both directions; many cases of vicious appendicitis are believed for twelve to twenty-four hours by good doctors to be food indigestion or belly-ache, tubo-ovarian pain, kidney colic, and other non-urgent conditions. Many normal or slightly diseased appendices are constantly being rushed to operation when the real trouble exists in other organs for which operation is either contra-indicated or could better be postponed to a suitable time or for which a better operation could be done. This observation is no new one. It's an old story, but no joking matter. So large a proportion of erroneous diagnoses have come to light either at the time of operation, shortly afterward, or by the next doctor who treats the patient, that most surgeons of studied experience have discontinued the practice of "emerging" within the first twenty-four hours of acute symptoms in any case of appendicitis save for most exceptional reasons.

Treatment before Operation.—In less than 10 per cent. of cases of appendicitis is the correct diagnosis made within the first twelve hours following the onset of the pain. No case to whom a cathartic had not been administered soon before or after the onset of pain, has had to be drained. No case who had morphine systematically adminis-

tered from the beginning of the disease has had to be drained. These observations were made several years ago, since which time I have had occasion to make observations in at least five hundred cases, many of which were deliberately carried along with a definite diagnosis (subsequently confirmed by operation), treated by avoidance of food, avoidance of purgatives and enemas, the administration of large quantities of water, and the use of adequate and repeated doses of morphine. I have not seen a single case which did not improve under this treatment; many have recovered completely from the attack, and others have gone to the formation of a perfectly walled-off abscess operated upon without mortality and with few disagreeable results.

The big fact standing out conspicuously in the records is that whenever a patient is seen for the first time with abdominal pain, if there is any question as to whether it is appendicitis (or as a matter of fact any other acute abdominal disease), the doctor should first administer a suitable dose of some opiate, preferably morphine, and specifically and emphatically order that no food and no cathartic of any kind be taken and no enema given. The patient should be seen again not later than six or eight hours, by which time the diagnosis is either definite or becoming so. I have never seen a case of acute abdominal pain caused by surgical pathology which was not made worse by the administration of cathartics and food, nor one which was completely relieved by a single dose of morphine. This leads to the belief that immediate and proper treatment of symptoms is of great value in making possible a correct diagnosis and in preparing the patient for operation.

At this point I am reminded that much animated opposition has been expressed against the use of morphine for abdominal pain, and, while most doctors give it, some few actually do not like to give it for fear it may mask symptoms and cause the patient to refuse to be rushed; others have withheld opiates until the diagnosis was made and then given a dose or so to quiet the patient for the trip to the hospital. From these and others in whom operation was postponed and opiates given during the interval of waiting, it was very clearly apparent that when appendicitis was the trouble the pathology also was usually masked, often adequately quarantined. A great many of the thousand cases in this series have been brought for operation to Richmond from distant counties in Virginia and neighboring states and it

has been uniformly testified by patients, their friends and doctors who have accompanied them, that the patients were never worse after the trip, and usually appear better than when they left home. During the trip they have not taken food and have taken morphine.

In every case of appendicitis the question of *immediate* or *postponed operation* must be answered. The reasons for postponing operation upon patients whose symptoms and signs are of moderate severity and stationary or subsiding will be answered upon the basis of the whole patient, considering what else may be the matter and the personal individual situation.

Though in between 75 per cent. and 90 per cent. of cases of appendicitis in adults operated upon one or more attacks of acute symptoms has occurred and subsided before, this fact does not answer the question whether the present attack will do likewise. In most cases experienced doctors can feel pretty sure on this question after a few hours' observation. In others great care must be taken to distinguish between convalescence and the "fatal improvement."

What, then, is the true status of the factor of time in mortality? Do the records testify that plain ordinary time is solely to blame or that time combined with improper treatment are the mischief-makers? Who has seen a fatality or even peritonitis from appendicitis in a patient to whom no treatment had been administered and who has not seen the signs of appendicitis disappear completely (to recur later) with no treatment or bad treatment?

Concerning the duration of acute symptoms before operation, they vary in this series from twelve hours to three weeks and in adults acute attacks have been recurrent for months or years. We have very rarely seen a ruptured appendix within twenty-four hours after the initial pain and with great frequency have seen a slightly diseased appendix in patients who had been sick for days. There is strong testimony that the pathology is not guided solely by the hands of the clock and that the urgency for operation is less dependent upon the duration of the illness than upon the clinical picture presented. Careful observers and students of the subject are in thorough accord in the belief that the most dangerous operation a patient can have for abdominal pain is the "operation of purgatives in an attempt to move the bowels." We should never hear it said that any case of appendicitis proceeds to abscess and general peritonitis through the

effect of time alone. It is no longer open to doubt that the severity of appendicitis is much more intensified by the administration of food and cathartics than by the passing of time.

Applying this principle to the treatment of the disease, many thousands of cases have demonstrated before our open eyes that when peristalsis is pacified and other digestive functions inhibited by the withdrawal of all food, forbidding all attempt to purge the bowel, and the administration of ample doses of morphine, for any case of appendicitis, it is frequently proper, sometimes wise and in bad risk cases not rarely life-saving to postpone operation even after the patient has been placed in the proper hospital under expert care.

After it is determined that operation for the present attack is called for, the problem of immediately rushing the patient to the nearest hospital for emergency operation is one upon which much heated and prolonged debate of lively character has been expended. On the rostrum and in written articles surgeons often assert that they never wait longer than is necessary to get the water hot and the tools ready. This teaching has had great effect upon men of lesser experience, particularly during the years when they have not accumulated enough experience to change their natural tastes for dramatic practice, nor analyzed enough actual records to change their minds. After a while, however, we find that men's actions are not in fact what they think they'll be. How often have doctors found that after recognizing appendicitis and advising immediate operation the patient would for some quite legitimate reason decline to be operated upon, get another doctor, and promptly recover of the acute attack. And on the other hand, how often do doctors think the case is not one of appendicitis and treat the patient for some non-surgical or at least not urgently surgical trouble and find at operation, days or weeks later, that the patient was suffering all the while with appendicitis? In actual experience these observations are extremely common and in any group of a thousand cases will be noted scores of times with little, if any, difference in the results. Those who announce that they always practice immediate operation for all cases of appendicitis should quote the exact records and let us see whether they mean immediately after the onset of the disease or immediately after the diagnosis is made or immediately after they are admitted to the hospital. There may be great differences in the time of these three events.

Every doctor with much experience knows that to wait a reasonable length of time in any case to size up the situation is scarcely debatable and in 90 per cent. of cases is quite desirable. The wisdom of this is supported by experience in reducing errors in diagnosis, minimizing complications and lowering mortality. With a patient in good condition with or without abscess and the need for operation decided, it is not easy to find reason for more than a few hours' delay in starting the patient to the hospital for reasonably prompt operation. After this, when operation is deliberately postponed, the burden of proof as to the wisdom of this is upon the doctor who proposes it; and while it is generally safe and sometimes wise to postpone operation, it is imperative that ample morphine be administered, food withheld and cathartics scrupulously avoided until all signs have disappeared. With a certain type of case desperately sick with diffuse peritonitis and depleted by vomiting and purging, immediate operation, if not followed by death within twenty-four to seventy-two hours, has frequently left the patient in the same or worse condition than before the operation, with added local and general burdens. It is difficult to prove and not often true that because the "appendix has bursted and peritonitis has set in" the patient would have died if he had not been operated upon immediately; and if operation is followed by death we have lost the evidence and main witness in the case. Though many such cases recover after operation, complications are numerous and the mortality is high.

In no case in this series has the patient died under rigid application of the physiologic treatment preparatory to operation. This means no food, no lemonade, no cathartics, no enema; repeated and adequate lavage of the stomach contents; abundance of water by hypodermoclysis, by intravenous introduction, by mouth when it can be retained. The head of the bed may be elevated, soothing applications, preferably hot poultices or light ice-bags, are applied to the abdomen.

This treatment of bad risk cases is followed uniformly by improvement and, in the cases not actually moribund, has been followed within a week or ten days by walled-off abscess and the general condition sufficiently good to permit judicious feeding for a couple of days and a properly performed operation without further delay or preparation.

After operation, the same treatment with no interruption is con-

tinued as before. It is of life and death importance. Sixty per cent. of the deaths following operation for all types of appendicitis occur between the sixth and eighth days after operation and the second and fourth days after the enema and food. The records show that up to this time they did well enough, immediately following which they went bad. We must never forget that by the operation only the cause of peritonitis is removed and, when necessary, provision made for drainage. The disease in the unremoved peritoneum will be several days in undergoing resolution. Until this occurs there must be no relaxation of the life-preserving physiologic treatment. Before feeding we must recognize with certainty the differential diagnosis of convalescence from the "fatal improvement." Following operation they need no bowel action until a day or so after they eat, and by this time they usually will have it. The usefulness of rectal tubes and enemas in relieving pain and causing passage of gas before gas has been passed in large quantities spontaneously, is largely an imaginary effect on the part of an optimistic doctor or nurse. The record shows that the patient is made worse by pain, nausea and distention caused by stirring up of peritonitis. While recovery often follows such relapse, the fight is apt to be desperate. We may lose; and if we do, is not the loss chargeable, upon restudy of the record, to a relapse of peritonitis caused by too early administration of the enema which is terrible and food which is not worth it?

Problems of *operative procedure* are also lighted by the records. Of the total thousand cases, 715 were operated upon solely for appendicitis and its complications. In 285 the clinical history was that of a patient acutely sick with the symptoms and signs of appendicitis, but in whom there was a definite evidence of disease in other abdominal organs. If at the time of the operation for appendicitis pathology in other abdominal organs was suspected they were examined, and unless the appendix disease was suppurating, the disease of the other organs was treated as a part of the purpose of restoring the patient to complete health.

At this point the question arises, is this practice wise? This has not been routine practice in cases of suppurating appendicitis, though in a few instances it has been done without bad effect. In no case where this was done has a patient died, and in every case we have been gratified that all the pathology had been treated at one opera-

tion. The records of more than a thousand women operated upon primarily for pelvic disease show that 5 per cent. had at some previous time been operated upon by other surgeons for appendicitis and pelvic disease allowed to call for the second operation. The records further show that 5 per cent. of the women with appendicitis in this series had previously been operated upon by other surgeons for pelvic disease, at which time the appendix was allowed to remain and make needful the second operation.

Many surgeons have observed right inguinal hernia one, two or more years following appendectomy and some have attributed it to nerve-muscle injury through the side incision. Such a conception of the cause of hernia exhibits little appeal to the student of hernia, though it serves well to emphasize the need for discovering hernia when it exists in one who has appendicitis and calls for operative cure of the hernia at the same time appendectomy is performed, provided a time can be chosen when suppuration is not present.

In this series of cases of appendicitis a small number (less than 2 per cent.) also received operation for hernia. Since the problem is before us may we not do better? On the other hand, when operating for right-sided hernia in all but aged people I have for years removed the appendix through the hernia incision. And though we find it diseased in a surprisingly large number of cases these are not included in this report of the study of appendicitis. We do, however, include in this report approximately a dozen cases of vicious appendicitis in patients acutely sick, who had previously been operated upon for right-sided inguinal hernia and the appendix allowed to remain. In one case the patient believed his appendix had been removed at the time his hernia had been operated upon and on this account his appendicitis was not recognized until perforation had occurred.

A considerable proportion of cases operated upon solely on account of appendicitis have had other abdominal organs examined at the time of appendectomy. No case is included in this report in which the operation was performed primarily for hernia, gall-bladder, stomach or pelvic disease.

The low muscle-splitting McBurney incision for appendicitis and its local complications has so uniformly met the problem for me, that I have not enough records of other incisions for comparison.

This incision may be enlarged, if needful, by splitting the sheath of the rectus sufficiently to deal with any complication of appendicitis without cutting muscle-fibres. For exploration of other abdominal organs in cases where the appendix pathology is clean, midline or right rectus incisions may be essential.

In abscess cases the question, whether to remove the appendix or simply to drain, can also be answered by the records. Simple drainage has been employed in 24 (15 + per cent.) and the second operation always advised later after recovery is nearly complete. In 146 of 170 cases (84 + per cent.) the complete operation was performed at once. Death and stormy convalescence have followed both procedures, but in no case have I felt that either removing or leaving the appendix has been the chief factor of fatality. The exact thing to do in a given case will be dictated by surgical judgment and surgical skill. I have not had special difficulty in removing without added danger the appendix in 146 cases, though often in less neat fashion than might be desired, and have considered it unsafe to search for the appendix in twenty-four cases. I have thought it wise not to make prolonged or traumatic attempt to get the appendix in difficult cases of abscess adherent to the abdominal wall and may have unwisely allowed it to remain in some. Adequate exposure, great gentleness and moderate speed have been the guiding principles of operative procedure.

In all cases not suppurating and in which suppuration is confined to the appendix and adherent omentum, the pathology can be removed with gentleness without spilling and without the need for drainage. Ancient adhesions tying the appendix down in deep locations may necessitate sharp knife dissection of the outer leaf of the mesentery of the appendix to facilitate delivery. The vessels of the meso-appendix are always contained in the inner leaf of the mesentery and are easily tied after division of the outer leaf, which is avascular. The artery in the wall of the base of the appendix shows when the appendix is stripped up sufficiently high and is tied with the base of the appendix at the cæcum. In a few rare cases it may be easier to make a subperitoneal or complete removal of the appendix from base to tip. In all clean and most abscess cases I have inverted the stump of the appendix base usually with linen suture. In certain cases requiring drainage, simple catgut ligation of the

appendix is ample and one hesitates to invite long-standing sinuses and fecal fistula by unabsorbable ligature and sutures. Every case commands very secure ligation, often by suture or a second tie of the vessels of the meso-appendix. No case of hemorrhage from this source has occurred in this series.

Walled-off abscesses should obviously be drained. Cases of regional peritonitis in which, even though the appendix is gangrenous, there is no fecal odor to the fluid, have been closed after the removal of the appendix and mopping up of the fluid. One such case died six days after operation of vicious colitis, without evidence of peritonitis or wound infection.

In the earlier cases gauze and rubber tubes were employed. As progress has been made in problems of drainage I have in the last few years employed only rubber-dam or soft tubes and in much less abundance. It is removed never earlier than the sixth to the eighth day and rarely put back. In no case has inadequate drainage seemed causative of death.

After operation the treatment is that of peritonitis upon physiological principles, *i.e.*, no food; no cathartics; no enema; plenty of water; plenty of morphine; plenty of gastric lavage until the belly is flat, gas and usually fecal matter pass spontaneously from the bowels and the patient is well (in clean cases usually for three days; in filthy cases five to eight, sometimes ten days). This is the treatment before operation; it is of life and death importance after operation. Its application is one of painstaking attention to detail in the spirit of faith in its efficiency and determination to save each case.

The length of time in bed has been in clean cases from three to seven days; drainage cases twelve to sixteen days, rarely three weeks.

Complications of serious nature exceedingly rare in clean cases are noted before, as well as after, operation in cases of extensive peritonitis. They are more properly designated post-purgation or peritonitic than post-operative complications.

Many abscess cases had signs of chest infection previous to the operation; two cases of subdiaphragmatic extension of appendiceal abscess, right basal pneumonia and pleurisy, recognized before operation, promptly subsided after operation. In one case, a boy twelve years old, the signs of pneumonia and appendicitis, both quite typical, appeared at the same time. With a temperature (due to pneumonia)

of 106° we deliberately carried the appendix along on preliminary treatment for a week for the subsidence of the chest pathology and then operated for appendicitis with abscess. In another we drained through the loin, through tubes below and above the diaphragm into an appendiceal and pleural abscess which had extended retrocæcally into the pleura and was being expectorated. One child with large abscess died of pneumonia (?) two weeks after operation. One death occurred from abscess of the lung four weeks after operation for appendiceal abscess.

There have been two positive and two doubtful cases of complete post-operative obstruction. The positive case occurred ten days following appendectomy and drainage of abscess. This case was operated upon through a median incision, the obstructing adhesions of the small bowel to the site of the abscess were released and high enterostomy was followed by recovery. Two other abscess cases in children received enterostomy the fourth and fifth days after operation; in neither case was the obstruction demonstrated and both died of the original peritonitis possibly hastened by the enterostomy. The records show that this error has not occurred since and many have recovered upon the physiologic "regulation" treatment of peritonitis. Second abdominal emergency operation upon patients with peritonitis is dangerous business rarely called for, and the cases here reported are the only ones upon whom I have performed it.

There were two remarkable cases exhibiting greatly exaggerated peristalsis and other signs of mechanical obstruction in patients sick a week with what seemed ordinary appendicitis. In both of these emergency operations were performed through median incisions, completely obstructing adhesions of small bowel to appendiceal abscesses were removed and enterostomy performed. One died that night. In the other, appendectomy and drainage were performed and he recovered after the most desperate fight for what appeared to be a dying man for several days. For this man's recovery the tenacious and intelligent efforts of the nurses and internes of the Memorial Hospital would seem to be responsible.

In one other case in a child with what seemed to be complete intestinal obstruction ten days after appendectomy and drainage of abscess, I was about to re-operate and when the child was anæsthetized there appeared what seemed to me to be impending death.

Without operating we placed in the colon through a rectal tube two quarts of hot water for whatever benefit it might be to a child in collapse and sent the boy back to bed. After fervent prayers by his mother all night, the child was well and his bowels loose the next day.

Five of the 170 drainage cases developed true fecal fistula after operation. All of these were large abscess cases, two in patients with obvious tuberculosis of the bowel and advanced disease of the lungs; three in children with large abscesses of two weeks' duration, complicated by actual or impending gangrene of the cæcum. One case healed spontaneously in three weeks. The two in tuberculous bowel cases never healed; in two the holes in the cæcum, and in one case in the small bowel, were sutured at the second operation.

There have been many cases of foul-smelling black discharge for several days following operation in abscess cases; some may have been true fistula, but in others the discharge appeared to be gangrenous material from about the appendix. It has comforted me to know that some surgeons consider cæcostomy advantageous in certain cases of vicious peritonitis. None of the fistula cases in my experience have died. Three other cases were operated upon for fecal fistula following drainage of abscess by other surgeons.

There have been three cases of femoral phlebitis in the thousand cases, all of the right thigh, all in men; two following operation in abscess cases; one following right rectus incision in a clean case—practically 2 per cent. of abscess cases.

There was one fatality due to infection of the veins and arteries of the abdominal wall and secondary hemorrhages shown at autopsy to be due to ulceration of the deep epigastric artery. This was three weeks following operation in an abscess case with extensive peritonitis. The peritonitis was all cured and the cavity clean at autopsy. Another abscess case complicated by similar secondary hemorrhage from the abdominal wall recovered.

One large abscess case was followed by annoying sinuses of the abdominal wall, which I attribute to infection of a blood-clot beneath the aponeurosis of the external oblique muscle. Recovery was slow.

One case of post-operative acute chorea developed in a child seven days after operation. Three days before the onset of appendicitis she had tonsillitis; emergency appendectomy was performed within

less than twenty-four hours; seven days after operation she developed violent chorea; two weeks later endocarditis.

One case ten days following appendectomy for acute symptoms of suppurative appendicitis, but without abscess, developed and recovered from a typical case of typhoid fever.

Deaths are more profitably studied in separate types of cases. Of 830 clean cases there were four deaths.

The first a woman with diffuse redness of the peritoneum and the appendix with symptoms of a few hours' duration following a week after tonsillitis in 1918. This is a type of case recognizable now by diffuse redness of the peritoneum, bowels and appendix resembling that seen during the epidemic of influenza. I would call this an error in diagnosis with no need for operation. She seemed no better after than before operation; she seemed no worse for two days after operation. Imperfect attempts were made to move the bowels and liquid food given beginning the third day. She promptly became worse and died on the eighth day of either peritonitis or obstruction, or both.

The second clean case, a child, three and a half years old in 1920, died after operation for questionable symptoms of twenty-six hours' duration, the operation showing pathology similar to the case above. There was no pus; she died the next day in stupor and collapse. Since this I have not operated upon a child under four years of age unless there were unquestionable evidences of suppuration.

The third clean case, a man in 1922 died of violent colitis starting the third day after operation for gangrenous appendicitis. This was a most vicious colitis such as I had not seen or heard of before nor until 1924 when some cases were reported from Mount Sinai Hospital, New York.

The fourth clean case died in 1923 following repair of post-operative rupture and the removal of the appendix three years following drainage of abscess. He was fat, over fifty years of age, and the operation was rather difficult and prolonged; during the first night, while apparently in good condition, the nurse suddenly noticed him stop breathing.

Of 170 abscess cases with and without spreading peritonitis there were seventeen deaths.

There were nine deaths from spreading peritonitis operated upon while the disease was in the advancing stage. Five of these died within from four to twenty-four hours; one after fifty-five hours; two between seventy-two and ninety-six hours; one lived a week after operation. Three of this type were boys; two, four years old; one, thirteen; and one a man over fifty, treated continuously for years for cardiac disease.

The other four of this group were healthy young men and women desperately sick but appearing capable of standing an easy, gentle "touch and go" appendectomy and drainage by which they were in no way benefited.

There were eight deaths (5 + per cent.) of the 130-140 cases of abscess, perfectly or imperfectly walled off with peritonitis limited to the region.

All of these did quite well for three or four days after operation when the enemas and food were given. Five went from bad to worse immediately after

the enema and died a peritonitis death two to four days later. In three of these we did useless or harmful enterostomy about a week after the first operation.

Two abscess cases died two weeks and four weeks, respectively, after operation, with the abdominal situation under good control. One a man, thirty-three years old, with pneumonia and what appeared to be abscess of the lung, in the fourth week; the other a boy, fifteen years old, with pneumonia and pleurisy, after two weeks.

The remaining death among abscess cases was on the twenty-first day following operation upon a woman, thirty-eight years old, who had a normal convalescence until the eighth day, when chills, fever and phlebitis of the abdominal wall appeared, followed later by repeated small hemorrhages from the abdominal wall and finally death on the twenty-first day. Autopsy showed normal organs and no residual abscesses in the peritoneal cavity, but with demonstrable ulceration of the deep epigastric artery. This was unique up to that time (1920). In 1924 several such cases were reported by Wilenski from Mount Sinai Hospital, New York.

And now may we not offer for discussion the following resolutions:

- (1) To any patient with severe abdominal pain liquid food is harmful; solid food is dangerous.
- (2) To attempt to purge the bowels is a pernicious practice.
- (3) Purgative medicines should be removed from the family medicine shelf. Laws similar to those against narcotics and alcohol should prohibit the sale of cathartics except upon prescription, and prohibit the treatment of patients with abdominal pain by any but qualified doctors of medicine.
- (4) People should be taught to call promptly a competent doctor for every case of severe abdominal pain and to take no medicine, save possibly a single dose of paregoric, and no food before the doctor arrives.
- (5) Every doctor should regard calls to patients with abdominal pain as emergency calls to be answered with great promptness, commanding painstaking study at intervals of not more than six or eight hours until the pain and other symptoms are completely relieved, or a working diagnosis made.
- (6) The correct diagnosis of the exact cause of severe abdominal pain within the first few hours of its onset is possible but rare. When labelled appendicitis and operation performed or when labelled not appendicitis and operation not per-

formed, the errors in diagnosis in both directions will total fifty-fifty.

- (7) The immediate treatment of symptoms and repeated examination of an acutely sick abdomen for the first few hours is of greater importance than exact diagnosis, will diminish the number of errors in diagnosis, and will permit the substitution of therapeutic for exploratory operations.
- (8) The permanently curative treatment of appendicitis is admittedly by surgical operation. There is no proof that the policy of pushing, shoving and rushing patients to the nearest operating table is ever necessary or generally wise.
- (9) There is no place in the management of appendicitis for hysterical excitement and theatrical performance.
- (10) The whole course of treatment of appendicitis in most cases may be very simple and safely carried out. In others it may be extremely difficult and dangerous, entailing the need for the solution of big problems and the performance of operations of great magnitude. In every case the rigid application of physiological treatment should be applied from the moment of onset of the symptoms before, during and after operation until the patient is well on the road to complete recovery.

No case of appendicitis is so simple that the patient may not die, and no one not yet moribund is so sick that the man, woman or child undergoing treatment may not recover from the attack.

BLOOD DILUTION IN THE PATHOLOGY AND TREATMENT OF ATTACKS OF GOUT

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FOR THE estimation of uric acid we employed Grigaut's modification of Folin's technic. Folin's procedure has been recently criticised by Mathieu, Weil and Guillaumin, in that they believe that by it the expression "total uric acid" applied to substances submitted to quantitative analysis by this technic in the total volume of blood is not exact, because it does not reveal the total amount of uric acid and other substances chemically distinct from this acid.

Although keeping in mind these objections, I nevertheless believe that Folin's procedure gives a sufficiently exact clinical idea of the tenor of uric acid in the blood and that the results I have obtained in eighty cases would not be essentially different had another technic been employed.

The normal amount of uric acid in the total quantity of blood in an adult averages nine centigrams per 1000 c.c., and all observers who have estimated the quantity of uric acid in the blood—by no matter what technic they used—have come to the conclusion that the gouty subject is invariably hyperuricæmic. Taking the eighty cases of gout we have studied, I find that fifteen centigrams of uric acid in the total blood represents the average amount. All my cases were distinctly uricæmic, no matter what was their condition of renal permeability.

This fact has been placed in evidence by Professors Chauffard, Brodin and Grigaut in their early researches. In my personal dosages I have noted that the ratio of uric acid in the plasma to that of the total blood varied enormously. The normal ratio is about $\frac{1}{2}$; that is to say, in a normal subject on a normal diet, the tenor of uric acid in the total blood being nine centigrams, the tenor in the serum is four and a half centigrams. In extreme cases, as I shall show, this ratio varied from $\frac{1}{4}$ to 1. Thus, in Case 80, there were seventeen centigrams of uric acid in the total blood and four and seven-tenths centigrams in the serum. On the other hand, in Case 1, there were

twelve centigrams of uric acid in the total blood and thirteen centigrams in the serum. In estimating the ratio of the amount of uric acid in the serum multiplied by 100, with the amount of uric acid in the total blood, the extreme figures of my contents are 108 and 27. It is to be remarked that the variations of these ratios are independent of the percentage of uric acid. Thus, for example, for thirteen centigrams of uric acid in the total blood I find in seven of my cases that the amount of uric acid in the serum greatly varies, as may be seen by the following table:

<i>Uric Acid</i>				
	Total Blood	Serum		Ratio
Case 2	0.137	0.147	=	108
Case 9	0.139	0.134	=	96
Case 11	0.139	0.103	=	74
Case 17	0.132	0.080	=	62
Case 21	0.138	0.074	=	54
Case 29	0.134	0.073	=	54
Case 56	0.139	0.062	=	44

These variations, which were first shown to exist by Rouzaud and Thierry, are in direct relation to the viscosity of the blood, as I shall now attempt to show.

To estimate the relative tenor of serum and globules in the blood, I have employed Hess' viscosimeter, but certain factors intervene which modify the results. Thus, a distinct increase of uric acid, cholesterin or biliary salts increase the viscosity and this increase is especially evident for the sugar of diabetics. But these various elements do not pervert the ordinary parallelism existing between viscosity and the tenor of globules in the blood.

The best procedure to estimate the ratio of globules to the plasma is centrifugation of the blood after having been rendered uncoagulable in a graduated tube. I have frequently compared the results obtained by centrifugation with those of the viscosimeter. They are concordant and, in practice, the viscosimeter gives correct data in respect to blood dilution. In the particular study under consideration we obtained our data from blood taken by needle-prick. Its color and consistency, its more or less rapid flow, already allowed one to roughly estimate the relative richness of the blood in globules. I would here remark that the figures given by the Hess viscosimeter

correspond quite closely with the tenor of globules in the blood reduced to one-tenth.

Normal viscosity is 4.2. The tenor of globules in the blood is usually from 4 to 4.5 per 10, and in fact the amount registered by the viscosimeter approximately gives the ratio of globules to the plasma.

There is no direct relation between the amount of uricæmia and blood dilution. Thus in my Case 1, a uræmic subject with extreme blood dilution: Viscosity equals 1.9, there was the same amount of uric acid in the total blood as in a patient (Case 29) with a normal viscosity of 4.3, and in a subject with high viscosity of 5.4 (Case 50). All three patients showed twelve centigrams of uric acid in the blood.

Consequently, with a very variable tenor of globules in the blood, the amount of uric acid may be the same and inversely, for the same degree of viscosity, the amount of uric acid may be very different from one case to another.

As uric acid is found in greater proportion in the globules, a subject with a high viscosity will usually have a high percentage of uric acid but there need not be any parallelism between this viscosity and the total uricæmia. On the other hand, what is very evident is that the ratio of the uric acid in the serum with the uric acid of the total blood varies inversely to the viscosity: In my cases this ratio of 108 for a viscosity of 1.9 to 27 for an extremely high viscosity of 8.9. The higher the blood dilution, the greater is the relative proportion of uric acid in the serum, and this is true no matter what the total uricæmia may be.

So far I have attempted to show that a gouty subject is a uricæmic and that uric acid will be found in greater amount in the serum in relation to the same quantity in the total blood, the higher be the blood dilution. I now wish to show the interest that this fact presents in the pathogenesis and treatment of attacks of gout. But before entering the domain of hypothesis, and keeping in mind the criticisms made in respect to the method of estimation we employed, we wish to give six case histories which are, we think, conclusive.

CASE I.—Male, *æt.* fifty years. First attack of gout in 1912. In 1918, 1920 and 1921, the patient went to Vichy and soon after beginning his hydromineral cure he developed attacks of gout. The viscosity was estimated for the first time during the third attack at Vichy (July 25, 1921) and was distinctly low, being 3.9. The blood-pressure taken with a Pachon was maximum, 20; minimum, 12.

Patient was ordered to rest up and was put on a dry diet. The Vichy treatment was also stopped.

On July 27th, the viscosity was distinctly higher than the average, being 4.8. The dry diet was continued, a daily hot-air bath was ordered and the hydro-mineral cure was again resumed.

From July 27th to August 15th the patient ingested 500 c.c. of Vichy water per day.

August 3rd: Viscosity, 5.1. Blood-pressure: Maximum, 19; minimum, 11.

August 15th: Viscosity, 4.6. Blood-pressure: Maximum, 17; minimum, 10.

The attack of gout retrogressed at once after beginning the dry diet and did not recur, and the patient took his Vichy cure perfectly. He continued the dry diet. He had no attacks in 1921 and 1922.

Blood examination in April, 1922, gave: Blood-pressure: Maximum, 20; minimum, 12.5. Viscosity, 6.4. Urea, 0.37. Residual nitrogen, 0.17. Uric acid, 0.156 total blood. Uric acid, 0.053 serum. Glycæmia, 1.22. Cholæmia, 1/22,000. Cholesterin, 2.68 total blood. Cholesterin, 2.01 serum.

Analysis of urine: Distinct albuminuria; urobilin in excess; uric acid, 0.89; urea, 21.05; ammoniacal nitrogen, 0.78; Maillard's coefficient, 7.9; Ambard's, 0.096; ratio of uric acid to urea, 4.2.

This is, briefly, a case of gout developing attacks with each hydromineral cure when on ordinary diet, but these do not occur when on a dry diet which increases the blood viscosity.

CASE II.—Male, *æt.* thirty-one years. Gout from the age of twenty-four. The attacks have been frequent and the patient is impotent most of the time.

He arrived at Vichy, June 24, 1921, walking with canes, with painful swelling of both knees and ankles. Blood-pressure, maximum, 16; minimum, 10.

Blood examination: Viscosity, 3.6. Urea, 0.35. Uric acid, 0.182 total blood. Uric acid, 0.127 serum. Cholesterin, 2.22 total blood. Cholesterin, 2.22 serum. Glycæmia, 1.27.

On account of the very low viscosity he was ordered a diet containing a large amount of sugar with a reduced quantity of fluids. A drastic purge was given on two successive days and a general light bath, with hot-air baths over the knees.

June 28th, blood examination: Pressure, maximum, 18; minimum, 10. Viscosity, 4.6. Urea, 0.32. Uric acid, 0.176 total blood. Uric acid, 0.103 serum. Cholæmia, 1/25,000. Cholesterin, 2.31 total blood. Cholesterin, 2.13 serum. Glycæmia, 1.28.

In four days the viscosity went up from 3.6 to 4.6, the other elements in the blood remaining practically the same. The Vichy treatment, at the dose of 600 c.c. of water, was continued for three weeks. The attack of gout rapidly retrogressed and in a few days the patient walked without canes. Seen three months later he had been free from any attack.

This was a gouty patient whose attack rapidly subsided during a hyperviscosifying diet and tolerated perfectly the alkaline treatment at Vichy. The ease with which the viscosity was raised and the excellent effect of a dry diet, which was continued by the patient, are to be noted.

CASE III.—Male, *æt.* forty-nine years. Enteritis and migraine in childhood; first attack of gout at the age of thirty-six. During treatment at Vichy in 1909 and 1910, he developed attacks of gout in both knees and left foot. Seen in

August, 1921, the viscosity had reached 4.3; blood-pressure, maximum, 19; minimum, 11.

On a dry diet this patient was free from attacks during a cure of 500 c.c. water daily at Vichy. During this cure the viscosity remained above normal, successive examinations giving: 4.5; 4.2; 4.7 and 4.6.

This patient was able to tolerate the alkaline cure at Vichy after he had been put on a dry diet.

CASE IV.—Male, *æt.* fifty-nine years. First attack of gout at the age of forty-eight. Four cures at Vichy from 1913 to 1917, each of which caused gouty accidents to develop. He next came to Vichy in 1921. At this time the blood-pressure was: Maximum, 17.5; minimum, 10.5. Viscosity, 3.8. Blood-urea, 0.37. Residual nitrogen, 0.156. Uric acid, 0.154 total blood. Uric acid, 0.95 serum. Glycæmia, 1.48. Cholesterin, 2.34 total blood. Cholesterin, 2.46 serum. Wassermann, +.

Put on a dry diet, the patient tolerated a three weeks' cure at Vichy, taking 400 c.c. of water daily. When he came the following year with a viscosity of 3.4 and without taking any precaution in diet, he developed an attack of gout on the second day of treatment.

In this case the patient developed attacks of gout during treatment at Vichy four consecutive years but at his fifth cure on a dry diet no attack occurred, while at the sixth cure without attention to diet he developed an attack two days after beginning to take the Vichy waters.

CASE V.—Male, *æt.* fifty-six years. First attack of gout at age of forty-one, frequent ever since. Came to Vichy in 1921 and developed several attacks. Blood examination on arrival: Sp. gr., 1052. Viscosity, 3.1. Blood-urea, 0.52. Uric acid, 0.134 serum. Uric acid, 0.139 total blood. Glycæmia, 1.75. Cholæmia, 1/30,000. Cholesterin, 2.22 serum. Cholesterin, 2.28 total blood.

On the following day a generalized attack of gout developed and lasted twenty-three days.

This was a case of gout with renal insufficiency and low viscosity, developing a serious attack of gout on account of this low viscosity.

CASE VI.—Male, *æt.* forty-three years. First attack of gout at the age of thirty-three. In July, 1921, after having been free from attacks for eighteen years, the patient took a cure at Barbazan which set up a violent attack of his disease.

On his arrival at Vichy on August 9, 1921, the attack had not completely subsided. Viscosity, 3.7; blood-pressure: Maximum, 18.9. Regardless of this very low viscosity the patient immediately began his cure, having been put on a dry diet and light baths. During the hydromineral cure the viscosity was 4.7 on August 10th, and 4.9 on August 27th.

The attack rapidly subsided and the cure at Vichy was carried out without accidents.

This is a case of a subject with low viscosity who developed an attack of gout during a hydromineral cure and who tolerated an alkaline cure during this attack by raising the blood viscosity.

I have chosen these six cases because they are typical, although I have notes of many similar instances. From these case histories it seems clear that the increase of the blood dilution or, what amounts

to the same, decrease of the viscosity, accompanies an attack of gout in a gouty uricæmic subject with normal or low viscosity. By raising this viscosity in patients who, during previous alkaline treatments (which reduce the viscosity), developed attacks of gout, this treatment can be carried out without any accident. Hypoviscosity exists in gouty subjects at the time of an attack of gout, and these patients with hyperviscosity only develop attacks of their disease when a slight drop in the viscosity takes place.

To the cases we have been considering, I could add a great number of previously gouty patients who have become diabetics, who present a very high viscosity and are free from their gout. I am convinced that the blood dilution is of great clinical importance as well as for treatment, as I shall attempt to show.

The question arises as to why a uricæmic subject should develop an attack of gout when the blood dilution increases, but before answering this it may be well to ask if other factors than a high blood dilution may not intervene in an attack. I think I am right in saying that all the causative factors of attacks of gout may be regarded as playing a part on account of the increase of this dilution. I am unable to offer a direct proof of this assertion by the degree of viscosity before and after the action of these causative factors, yet I believe it is logical to admit that the ordinary causes are susceptible to provoke attacks because they increase the blood dilution.

The ingestion of large amounts of liquids and large meals unquestionably act in this way. Cold, alcohol and alkaline waters (such as Vichy) attain the same result probably by the intermediary of renal congestion which lowers the viscosity by producing hydræmia.

From this viewpoint the kidney plays an important part. In gouty subjects with renal insufficiency there is far more danger of attacks arising because they are predisposed to crises of hydræmia.

On the other hand, the salutary effect of profuse sweating and diarrhœa on an attack of gout is well known, and I could mention several cases where improvement began when diarrhœa developed. Now, sudation and diarrhœa are two great factors in removing the water from the blood, hence inducing hyperviscosity. Therefore, I believe that the variation in the tenor of water in the blood is an essential etiological factor in an attack of gout and that the ordinary causative factors of the attack act by the intermediary of the former.

Now, as to the pathogenic interpretation of the part played by blood dilution in the attack, we have seen that uric acid, no matter what its tenor in the blood may be, is all the higher in the serum the lower be the viscosity. Chauffard has pointed out that the uric acid of the plasma is probably that which intervenes in the gout attack, and this opinion has been sustained by the researches of Weil and Guillaumin. According to these observers the uric acid of the plasma is free at 9/10, while the uric acid of the blood-cells is almost totally combined with albuminoid substances. Without taking into account the ratio existing between the uric acid of the plasma and that of the total blood, as proposed by Rouzaud and Thierry, the very great number of dosages I have made allows me to affirm that the free uric acid of the plasma very distinctly increases when the blood dilution itself becomes higher and this increase is considerable. To ascertain the total quantity of uric acid in the plasma, one must take into account not only the tenor of uric acid per 1000 c.c., but also the tenor of the plasma in the blood.

I have already said that the Hess viscosimeter was a convenient instrument giving sufficiently exact results in respect to the tenor of plasma in the blood. Let me take an example from my eighty cases. The patient in question had a viscosity of 1.9 per 1000 c.c. of blood and thirteen centigrams of uric acid in the plasma plus $\frac{8.1}{10}$ or 0.105. Let me take another case in which the viscosity = $8.9 \text{ to } 0.047 \times \frac{11}{10}$; otherwise 0.00517 in the plasma per 1000 c.c. of blood.

It will therefore be seen from these extreme cases of uric acid in the plasma that it may vary in vast proportions—from 0.00517 to 0.105, otherwise put, from 1 to 20. One can conceive how these variations may assume importance in the accidents of gout if it be really the almost free uric acid of the plasma that intervenes in the humoral phenomena of the attack. The blood dilution provokes the attack of gout by increasing in proportions which, we have said, may be considerable, the uric acid of the plasma.

Whatever may be accepted as far as the preceding pathogenic hypotheses are concerned, I wish carefully to separate the clinical data that I have recorded. On the one hand, it is essential to set up an elimination of uric acid in gouty subjects. For this it is logical

to increase the percentage of uric acid in the urine—for an equivalent amount of uric acid circulating in the blood—by diuresis cures and direct action on the liver. On the other hand, I have attempted to show that by diluting the blood, there is danger of provoking attacks of gout in hypoviscous subjects. Therefore, the treatment of gout must be conducted from a double standpoint.

The state of blood dilution, measured by the viscosity or any other means, should be first of all noted. In gouty hyperuricæmia with hyperviscosity, a diuretic cure or an alkaline course of treatment will not lead to accidents and may be undertaken without reserve.

In the hyperuricæmic gouty subjects with normal or hypoviscosity, a cure should not be undertaken unless the viscosity is raised by the ready and easy means of a dry diet. It is also the best means of rapidly controlling an attack of gout. The hyperviscosing regimen may be likened to a barrage of uric acid in the circulation, and is a ready means for doing away with the rather too potent action of a hydromineral cure in the elimination of uric acid. It controls the accident and not the gout itself.

With a knowledge of the state of blood dilution the practitioner will derive the necessary and proper indications for the therapeutics for increasing the elimination of uric acid and oppose its accumulation in the organism, at the same time avoiding an acute access of gout. By proposing a study of the blood dilution in gouty subjects and the dry diet as a prophylactic or even curative measure in attacks of gout, one must not overlook the treatment of the disease itself.

THE DEVELOPMENT OF PSYCHIATRICAL RESEARCH *

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A SURVEY of the development of the science of psychiatry discloses a series of stages, characterized by sweeping revolutions of the prevalent views and methods of research. The earliest development of psychiatry is lost in the gloom of superstitious ideas on the nature of mental disease. The morbid symptoms, as far as they were apprehended, were regarded as demoniacal, and were fought with means, which were considered efficient to counteract the demons. Exorcisms, charms and symbolic rites chiefly were in vogue. A remnant of this phase of development is still seen in the belief that people were possessed, and occasional exorcisms, which have persisted up to our times.

A new stage in the development has been effectuated by the formation of a real medical science. Instead of the belief in demons, disease was gradually recognized as the cause of madness and that, to a certain degree, it is comparable with other illnesses of the body. Even as late as 1835, the doctor and poet, Justinus Kerner, believed that a prophet sent by God would discover among the infirm in the lunatic asylums, some really possessed, who could be healed by exorcism. However, the medical view has long since prevailed. This led to looking for the causes of mental disease in various bodily maladies, as is indicated by such expressions as hypochondriasis, melancholy, phrenitis and the like. The sorcerer was gradually replaced by the physician, who endeavored to fight the disease by a variety of bodily and mental remedies. Naturally attention was drawn only to the more severe and conspicuous forms of madness, especially insofar as they were accompanied by bodily derangements, fever, paralysis, fits, etc. In numerous cases, however, morbidity was not entirely recognized, especially where it involved gradation of the normal state of health only. Frequently a moral or a religious explanation took the place of medical diagnosis. We best

* An address delivered at Chicago during Professor Kraepelin's recent American trip, and received from him for publication November 28, 1925.

see this in the proceedings against witches, in which doubtlessly many a harmless lunatic was regarded and treated like a cursed criminal. On the other hand, morbid trances were declared as the emanation of divine influences.

Though from antiquity a gradually increasing medical comprehension of the phenomena and nature of mental disease has been acquired, we can by no means speak of a profound conception of the pathology of disease. This is chiefly explained by the circumstance, that the individual physician had but little chance to collect personal experience with the insane. Chiarugi towards the end of the eighteenth century had published a collection of 100 cases of mental disease. We may infer that it contained the essential part of his experience. We know that Autenrieth wrote his first psychiatric work after having watched a total of fifteen cases of insanity. The reason for this insufficiency of data is to be found in the lack of lunatic asylums, and the infrequency of insanity. Only insofar as the cases seemed dangerous or inconvenient, were they given scanty if any medical aid and accommodated in poor-houses, work-houses, infirmaries or even prisons. At but a few places did the insane receive hospital treatment, which gave some doctors the chance of collecting more complete experiences on the phenomena of mental disease, its causes and course. Under these circumstances methodical investigation of insanity can scarcely be spoken of. Therefore the scientific publications mostly contain reports on special outstanding observations or general discussions. In many cases they merely propagated the opinions of the older physicians.

A decisive turn in these conditions came with the foundation of regular lunatic asylums and the development of the profession of an alienist. Though in the eighteenth century and even earlier medically advised sections for the insane have existed in hospitals, regular care for the mentally diseased commenced at the end of the nineteenth century, and it has taken several decades to procure an adequate number of medically managed institutes for housing, nursing and treating the mentally diseased. Soon a number of men were found, who made the care of the insane their profession. They had the opportunity of observing for longer periods numerous cases brought to them. They naturally soon felt the need of systematizing their observations, deducing certain doctrines from them, and collaborating

with their professional colleagues. Thus, soon after the beginning of the nineteenth century, the first psychiatric reviews were published, which, to be sure, in accordance with the spirit of the times, were often full of discussions on natural philosophy. They also contained extensive coherent compositions covering the whole scope of mental disease and especially striking phenomena.

The psychiatrist of that time was reduced to the expedient of observation at the sick-bed. Naturally he lacked all the improvements which render the other branches of scientific medicine productive. Psychiatric knowledge was, therefore, chiefly restricted to descriptions of impressions, which were immediately furnished by daily observation. The classification of phenomena and the grouping of mental diseases had no guide other than the outward manifestations of insanity, and the consideration of symptoms. Naturally the desire arose to account for the causes of the disease. As an intimate comprehension of the character of these complaints was lacking, the theories of the causes could be based on only superficial connections, as they seemed to present themselves by everyday experience. Thus quite casual incidents sometimes were taken to be of causal importance. To a great extent the manifestations of the diseases were viewed as original causes, especially insofar as they preceded the more striking morbid derangements. The same tendency appears in connection with the self-accusations of the melancholics, regarding their sinfulness as responsible for the outbreak of their illness. The uncertainty in other branches of medicine as to the nature and causes of the diseases of the body had a strong influence on the psychiatric views. At that time, therefore, we find cited as causes of mental diseases all manner of physical and mental processes, of which from the present point of view, we recognize but a few as real causes of disease. I cite only the practice of cutting off the *plica polonica*, the curing scabies, obviating hemorrhages, measures which were looked upon as very dangerous to mental sanity.

Naturally the foundation of lunatic asylums made the observation of the course of mental diseases possible to a greater extent. The only method at command, observation of the phenomena, at that time did not allow of classification of pathologic processes. The connection between the manner in which the case ended and its nature remained unexplained. The individual psychiatrist, to be sure, could

on the ground of his observations form certain and often judicious presumptions on the further course of the disease under treatment, but he was quite unable to prove his theory or to set up rules, by which, in future, other physicians might form a judgment of the presumable termination of the several forms of mental disease.

Post-mortem examinations, which had had such brilliant results in other departments of medicine for the comprehension of the most diverse diseases, could not help the psychiatrist very much in his endeavors. It is true that the changes in the brains of paralytics were known comparatively early, though only in outlines. However, the rest of the manifold and ambiguous findings, which certainly for the greater part had no connection with the mental diseases, were unable to throw light on the nature and origin of the morbid processes at the bottom of mental diseases. The scientific work of the ancient psychiatrist ended with careful, often marvellous descriptions of all the phenomena of insanity, with which he became acquainted in the course of everyday experience. He had not attained a profound comprehension of the actual processes, nor was he able satisfactorily to collect his observations into a coherent doctrine.

A certain importance for the development of psychiatric science is under these circumstances to be attributed to the creation of clinical institutes devoted to the education of the rising generation of physicians, and which had long been aimed at by the psychiatrist at the university but without success. Firstly, the function of teaching imperatively demanded the systematizing of the experiences and the setting up of doctrines to enable the professors to convey the knowledge to the students. From this purpose numerous descriptions in the way of compendia were issued, which show the endeavors of rounding off our knowledge and thereby clearing gaps in our science.

With the new institutes established in the second half of the nineteenth century at the various universities, it was of particular moment that they entered into relations with the other branches of medicine and immediately partook of their progress. More especially it was the theory of the brain and nerve diseases which fertilized psychiatric research. Here, from various causes, the conditions for profoundly comprehending morbid processes were much more favorable. To recognize the type of the derangement in a certain case was much less difficult than explaining complex and

heterogeneous phenomena of insanity; on the other hand, the opening of the bodies gave findings which were unmistakable and recognizable without special expedients, the derangement in life thus being easily explained. Such experiences naturally tended to give birth to the urgent desire of also investigating more thoroughly the changes in the brain, which one had reason to believe to be the cause of mental disease. Thus pathological anatomy became the first auxiliary science to psychology, a science of which we had hoped to receive further elucidation on the nature of insanity. Wherever it was desired to cultivate further scientific aims besides watching the infirm, anatomical laboratories were established, in which by aid of microscopic research a more profound comprehension of morbid psychiatric processes was to be attained.

The work commencing in this province could only become productive after the preliminary conditions for establishing a more subtle pathological anatomy of the brain-tissue were given, by the discovery by Weigert and Nissl forty years ago of a range of methods of research. Hence a rich source of knowledge was opened, which has furnished us with the most important disclosures, and in our days is the chief resort for our comprehension and the outlining of numerous morbid processes.

A refinement of methods of research was engendered. Under the influence of Wundt a psychology founded on natural science was developed, and only by it were we enabled uniformly to estimate sick-bed observation. Up to that time the psychiatrists had been accustomed to avail themselves of the terms of everyday life, or to create a particular psychology which was not always intelligible to everybody. The progress of physiological psychology gradually, however, furnished a safe basis, on which a satisfactory grouping of the experiences and a common understanding could be achieved. Further it was possible, frequently with success, to revert to the methods of investigation of experimental psychology for morbid conditions. In some places psychological laboratories were established in the clinics besides the anatomical, and thus the equipment of the psychiatrist was increased by a new auxiliary science.

By far more valuable was the enrichment of the possibilities of research, which psychiatry derived from the utilization of serology, which had been developed by the researches on immunity. Though

in beginning it was only one branch of psychiatry, that of mental diseases caused by syphilis, which profited by serological investigation, the new help now has become very important. It has created the necessity of numerous special serological laboratories for psychiatric purposes. Endeavors have not been lacking to utilize new points of view, which resulted from the theories of serology, for one or the other purpose in psychiatry. Although a decisive success has not been recorded in this direction, it is unquestionable that a continuation of these researches on the extraordinarily intricate processes in the body fluids, especially in the blood, promises results also for our sciences. Recently attention has been called to the behavior of the blood glands under both sane and morbid conditions, which is not only of immense importance for the total capacity of the body, but also for all manner of mental processes. Here a new province of psychiatric research is being opened.

A further important link in the chain of psychiatric auxiliary sciences is the genealogical investigation, which recently has made speedy progress. Its importance for the comprehension of insanity and especially the science of its causes is ever increasing. Although it is quite an old wisdom that inheritance plays an important rôle among the causes or generation of mental derangement, it is only since the discovery by Mendel of the laws of inheritance that it has been possible to find those directives, which enable us more to profoundly enter into the connections in our domain. The productivity of this way of regarding the matter is so obvious that we simply cannot miss this auxiliary science of psychiatry.

As is shown by this short survey, quite regularly precise processes have served as turning-points in the development of psychiatric science, creating new conditions for the activity of the researchers. After the development of medical science had dislodged superstition regarding mental diseases, the next stages in the growth of the science were marked by the establishment of hospitals for the insane and the initiation of the psychiatric profession, and by the foundation of clinics, which were at the same time serviceable for teaching as well as for scientific investigation.

The question arises whether we have now reached the last possibilities for psychiatric inquiry, or, if not, what might be the course of further development of our science. The answer to this

question is not difficult to find, if we look at our recent progress. Obviously it is characteristic of the present stage that a series of auxiliary sciences have been formed, by the coöperation of which, with clinical observation, we have attained extraordinary progress in the course of few decades. This development has, as will be seen, entailed far-reaching division of labor, and has had the consequence that nowadays no single scientist is able to view, or, what is more, to master the entire field of psychiatry. Therefore the need arises everywhere of training special persons for the cultivation of the several auxiliary sciences, the number of which very likely will increase in future. It is evident that such an extension of our province demands entirely new organizations. If up to the present time, one or the other assistant was occupied for a time with the research in an auxiliary science, he was forced to work at the same time in the other branches, especially in clinical psychiatry. If he did not want to endanger his future career, it became necessary, if possible, to return to that field after a certain time. Those who wanted to make the work in a special branch their life-problem had no possibility of attaining but a halfway satisfactory position.

From these arguments it follows that an effective promotion of psychiatric research is not possible under our present system. The endeavor must be made to found scientific institutes, which on the one hand are equipped with every expedient apt to help the researches of the different departments; on the other hand, to give a number of investigators, especially adapted to their work, the possibility of undisturbed and satisfactory occupation. With the great demands, which are even now put upon eminent clinicians with lectures and examinations, it seems necessary to free such institutes from the burden of holding lectures, in order to make all possible use of the scientific force. The new stage of development of our science will therefore be characterized by the foundation of research institutes as such have already proved to be efficient in various other provinces.

To be sure it will not be easy to establish such institutions. Where the government has undertaken to cultivate the sciences, it will have the necessary means only insofar as these endeavors at the same time promote education of the new medical generation. Parliaments usually look at purely scientific work from the viewpoint of costly amateurship. They are also restricted by the limits of their

economic capacity in making their appropriations to the greater extent for such purposes only. Under these circumstances a considerable part of the necessary means for research institutes will have to be raised by private generosity. Perhaps even more difficult is the discovery of suitable personalities, who are equal to their tasks and disposed to attain the utmost efficiency in their field of research. As such a specialization entails the renunciation and changes in the mode of living, it will be possible to engage eminent minds for this work only if positions for life are offered which permit of productively using their endowments and their living free of care.

Such a development is a pressing need. It must be urged and realized despite all difficulties. In many places an attempt to divide the labor has been made by creating superior positions for certain scientists of one or the other auxiliary branch. In Munich the attempt was even made in 1918, at first with the help of private donations, to establish a perfectly independent institute for research. In the beginning it was created for exterior reasons, to keep in intimate touch with the psychiatric clinic, which served the purposes of lecturing; however, from the very start, segregation of the institution from this connection was intended as soon as opportunity would permit. This plan so far has been thwarted by the breakdown of the economic structure of Germany. Naturally only certain sections could be created at first, as they corresponded to the most urgent needs and the forces at disposal. What will be the further development, the future will show.

In the research institute the clinical observation must naturally remain the base of the entire scientific work. The institute, therefore, in the first instance needs a ward for the patients, which need not be large, but must offer the possibility of a quick change of patients. It is of importance that this department should choose its material according to strictly scientific viewpoints. It must have the right of dismissing unsuitable cases quickly, and of retaining suitable ones as long as it likes and as medical considerations permit. At certain times it will be necessary to accumulate certain types of disease, which at the time govern the research in hand.

The number of the other institutes to be established depends on the needs of science and available forces. At the Munich institute an anatomical, a serological, a genealogical and a psychological section

were provided first. However, soon two other anatomical sections were founded, as we succeeded in engaging two eminent researchers, Messrs. Nissl and Brodmann, for collaboration. This procedure is characteristic of the institute. It does not establish a number of sections for special scientific branches, and afterwards search personalities fit to direct them. Our principle must be to first discover prominent scientists and then to give them the possibility of productive work, without regard as to whether or not other forces are occupied with the same problems. As every independent investigator goes his own way, such an increase of departments cannot be regarded as superfluous luxury, but, on the contrary, leads to an extraordinary enrichment of scientific collaboration as our unfortunately very short experience has taught us.

What the future extension of a scientific institute of research will be cannot be predicted. It is certain that, in the near future, quite a number of auxiliary sciences will be utilized. In the first place it will be necessary to found a chemical section, for which our preparations are already in progress. But it is very likely that later a single chemist will not be sufficient for the problems arising in the psychiatric province. The next task promising success is research on metabolism. Further, the need arise of studying more closely the chemical changes of the brain, in connecting with the different kinds of mental derangement. It is a question whether our present knowledge is sufficient to attack this problem with a chance of success. But in future it will of a surety play an important part, and then will very likely occupy an especially adapted scientist.

As a counterpart to the genealogical department which treats of the hereditary laws governing man, the section of biological inheritance will have to be established, with the task of breeding-experiments, investigating the questions of normal and morbid inheritance, as well as the injuries of the germ. Although such institutes already exist at certain places, it is beyond doubt that the special requirements of psychiatric research can only be satisfied by an institution working in intimate connection with the clinic on the one hand, and with the other departments of the Institute for Psychiatric Research on the other hand.

If at the present time the three anatomical sections had to be reduced to one, we shall nevertheless avail ourselves of every possi-

bility for further enlargement. Above all it will be necessary to establish a section for topographical cortical histology, as it has existed under the direction of Brodmann, and we shall do so as soon as we succeed in engaging a scientist suitable for this research. A division of labor for certain studies would be advisable. Comparative anatomy, embryology, inquiries into the processes in the brain, with the help of Gudden's method, sooner or later should be represented at an Institute of Psychiatric Research, likewise the pathological histology of mental diseases.

It is further evident that physiology must be among the auxiliary sciences of psychiatry. There is an urgent need to promote the theories on vital processes in the brain, also from the psychiatric point of view. The investigation of causes gives rise to a series of questions, which can only be answered by aid of physiologic research. The importance, more especially, of the sanguinary glands and the processes, normal and morbid, which go on in the fluids of the body, cannot be explained without the aid of the physiologist, who must collaborate with the serologist. The establishment of a physiological section must, therefore, be taken into consideration.

Another entirely different series of questions would have to be treated by a statistical section, which also must be provided in future. Its task would, to begin with, be to collect all figures apt to throw light on the causes and frequency of mental derangements in the population. Furthermore, an exact exploration of certain parts of the populace by the aid of census cards would have to be considered. From it much light could be thrown, especially on the question whether the symptoms of degeneration and insanity are increasing. This would be of utmost importance for safeguarding the mental health of the people. Here, naturally, collaboration with the genealogical section would arise.

It is useless at the moment to ponder on any further possible enlargements of the Institute for Psychiatric Research; I only want to mention that also comparative psychiatry and the history of our science belong to its domain. The example of serology has proved that unlooked-for new branches develop from the great tree of medical science and may attain unexpected importance. No man can foretell when and where this process shall be repeated. What we can at present introduce into our plans for the future is only a scaf-

folding, which must be constructed in a way as to allow of introducing new parts. As science is infinite, this development will never end. What will stay its progress is chiefly the insufficiency of available means which always will be in pitiful disparity to the size of the task before us.

The institutions I have here mentioned are meant to be seminaries for scientific students. To fulfill this claim, it is necessary, as has already been shown, to give scientists of eminent mental endowments the prospect of independent and economically satisfactory positions. They have got to be absolutely free in the pursuit of their scientific aims, and in disposing of their expedients. Further, they must not be detained from their life-object by obligations of any other kind. Nevertheless it would not be expedient to forego entirely the inciting effect of teaching the young. From general points of view it is desirable to attach the research institutes to the universities with their rich scientific incitement and resources and a restricted number of lectures will certainly be useful to the directors of the various sections. There will be the advantage of securing young coöperators in greater number and thereby giving them the possibility of selecting from them suitable assistants, who will later on be able to continue their mission.

What I have here characterized in general outlines as the most recent stage in the development of psychiatric research, is already more than a mere dream of the future. Although so far the only existing institute for psychiatry in Germany has had to suffer severely from the disfavor of the times, and cannot be improved at present as much as we might desire, during the time of its existence the German Institute for Psychiatry at Munich has nevertheless proven with certainty that the roads we have taken are practicable, and that they shall bring us nearer the aim of an ever-increasing perfection in our science.

THE TREATMENT OF METASYPHILITIC DISORDERS OF THE NERVOUS SYSTEM WITH INFECTIOUS DISEASES, IN PARTICULAR WITH RE- LAPSING FEVER

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THE discovery of the *Spirochæta pallida* by Noguchi in the brain of paralytics and the exhaustive research work carried out on its occurrence and distribution in the gray matter of the brain, with the aid of the improved methods of Jahnke, have proved that the presence of this microörganism in the nervous system is essential to, and in all probability the cause of, the development of general paralysis. It will scarcely be disputed that its destruction in, and elimination from, the nervous system would be followed by the arrest of the paralytic process. The elucidation of the intimate connections existing between the localization of the microbes and the occurrence of paralytic changes in the tissues naturally acted as a new and powerful incentive to the specific treatment of progressive general paralysis. Ehrlich's "606" and the allied arsenic preparations were administered anew in large doses, but without any response worthy of note being observed. The non-success of this specific therapy in general paralysis is one of the great riddles that besets the paralysis-syphilis problem. Must we ascribe this failure to a biological metamorphosis of the spirochæte which makes it resistant to salvarsan, or does the drug fail to reach the microörganism owing to its localization in the nervous parenchyma? Animal experiments have yielded a number of results that suggest the existence of a biological peculiarity on the part of the spirochæte in general paralysis, but up to the present time this view cannot be taken to be based upon a secure foundation. So much is certain, however, that even by circuitous means of the blood and spinal fluid barrier by introducing the "606" directly into the cerebrospinal cavity, the paralytic process fails to be appreciably influenced in a favorable manner.

This newer failure of specific treatment again centred interest

on non-specific therapeutics of many years' standing: Its essential foundation lies in the observation that the condition of paralytics improves if they suffer from any intercurrent, febrile disease. Quite a number of infectious diseases have, in the course of time, been found to be potent factors in this respect.

Experiments in this direction, originally carried out by nature, were copied in the fifties of the last century by Jacoby, while much interest was later roused by the publications of L. Meyer, who succeeded in causing extensive remissions in general paralytics by abscess treatment. This method, however, was soon afterwards abandoned, owing to the rather unfavorable results secured by other workers. We are indebted to Wagner von Jauregg, who employed bacterial products and dead bacteria, for a reëstablishment of non-specific therapy in recent years on a firm foundation. This author used chiefly tuberculin, which he injected in increasing strength, thus provoking a series of temperature elevations. The results obtained by Wagner von Jauregg with this method were good, and they were found to be improved if the tuberculin was used in combination with mercury and iodine. Other authors, however, including ourselves, were unable to obtain any encouraging results. Staphylococci, Streptococci, and typhoid bacilli, employed by the first-named author, also failed to be of therapeutic value in our hands.

At the Psychiatric Clinic at Munich we also extensively practised vaccine therapy by injecting typhoid, cholera, various mixed vaccines, and especially dead cultures of spirochaetes into paralytics, without, however, being able to observe any results worthy of note. The treatment of general paralysis with sodium nucleate, inaugurated by Donath and O. Fischer, which was thought by these workers to be productive of especially favorable results, owing to its causing a considerable hyperleukocytosis of the blood when introduced parenterally, was responded to only in a very moderate measure at our clinic and elsewhere. Other preparations customarily employed in non-specific treatment also failed to affect the course of the disease.

A new stage in this form of treatment commenced, however, when Wagner von Jauregg, in 1917, began to inject living viruses with a view to provoking genuine infections. He did this with the idea of occasioning a more intense systemic reaction and more frequent and higher temperatures than are obtainable by the introduction of dead

material. Malaria was the disease employed, and this therapy has in the meantime been successfully developed, not only at Vienna, but also at numerous other clinics.

On our part we are also in a position to comment favorably on malarial therapy. In approximately one-third of the cases we were able to observe extensive remissions, and have no doubt that the majority of them were due to the treatment applied. Unfortunately, we are unable to report on the duration of these remissions, as the fifty-six patients treated have only been under observation for two years at the utmost. For this reason, I am not giving any technical particulars or any notes on the course of infection with malaria, especially as these things are common knowledge, thanks to the numerous publications that have appeared.

It is my intention in the pages of the INTERNATIONAL CLINICS to discuss in detail another method of treatment, namely, treatment of general paralysis with relapsing fever, which we have carried out since early in 1919. The six years which have since elapsed now enable us to follow the fate of our patients. In coöperation with Steiner I commenced the relapsing-fever therapy of general paralysis in 1919, and we were originally guided by the notion that perhaps the therapeutical action could be intensified if a microörganism were employed that was more closely related to the syphilis spirochæte than that of the *Plasmodium malarix*. We reckoned with the possibility of the immunization bodies produced against the spirochætes of relapsing fever being able to influence syphilis spirochætes, as in the case of trypanosomal infections where the antibodies are not always exclusively directed against one certain species, immunity occasionally overlapping. The microbe used was that responsible for the African relapsing fever—the *Spirochæta duttoni*, as this was the only organism pathogenic for man which was at the time at our disposal in Germany. As a matter of fact, the relationship between the two spirochætes was demonstrated in a remarkable manner. The cell-count in the spinal fluid of infected patients rose to 1000 and more per cubic millimetre, with a concomitant rise of the quantity of albumin. At first we suspected that this accentuation of the liquor changes was due to an excitation of the syphilitic process in the pia, but it turned out that we were wrong, as the same manifestations could be noted when we infected dementia præcox patients. It was thus established

that the fluid findings were due to the action of *recurrens* spirochaetes in the cerebrospinal cavity, and it was further possible to demonstrate their presence and to study the inflammatory manifestations connected with their entry, by injecting the fluid into mice. *Recurrens* spirochaetes can be found in the spinal fluid during the second chill, and inflammatory symptoms subsequently set in. Gradually the latter die down, but the germs can still be found in the fluid after two or three months, not disappearing until after the inflammatory symptoms have long passed away. The spirochaetes of relapsing fever disappear from the blood at a much earlier date. As in the case of incipient syphilis, the germs invade the cerebrospinal cavity and cause meningeal irritations, which almost always remain clinically latent; only in three cases could a slight paresis of the facial nerve be noticed, which could possibly be interpreted as a neuro-recurrence.

The infectious material is taken from the tail of the mouse, or, preferably in the interest of sterility, from the thoracic cavity after the heart has been severed. The blood is subsequently mixed with saline and injected hypodermically or intravenously. In the same manner, blood of persons suffering from relapsing fever can be transmitted to other patients. No great difficulties are attached to the keeping of cultures of *Febris recurrens* and, as Illert has shown, such culture spirochaetes remain pathogenic for man. Outside the organism the blood remains infectious for mice several days, but only twenty-four hours for man.

The virus is best despatched in the form of freshly infected mice, or in the form of cultures. The incubation period after hypodermic injection is on an average five to seven days; according to our experience at least three days and *ad maximum* a fortnight. Intravenous administration reduces the time to two to three days.

Infection was unsuccessful in one of our cases only, so that natural immunity scarcely can be reckoned with. On the other hand, acquired immunity lasts for a very long time indeed. In no case were we able to re-infect patients, not even after the expiration of as long a period as $3\frac{1}{2}$ years. As a rule three to five chills ensue; the highest number observed was nine. The typical fever paroxysms take the form of very rapid rises of the temperature to 40° C. (104° F.) and more, with subsequent critical drops within twenty-four hours. The intervals between the febrile symptoms usually last six to eight days;

sometimes, however, they are considerably shorter or longer, and can even be four weeks in duration. Atypical temperature tracings are not infrequently met with; pseudocrises can occur as well as irregular intermittent temperatures which persist for a number of days. Owing to the length of the intervals that separate the chills, the fever does not exhaust the patient in any appreciable way. The disorder is absolutely innocent in its course and does not imperil the patient at all. Herpes labialis is commonly observed; on rare occasions a slight jaundice was manifest, while enlargement of the spleen was encountered in practically no case. Antipyretics should be avoided, while cardiacs—digitalis preparations or strophanthus—should only be resorted to in exceptional cases.

The disease is allowed to come to a natural end within some six to eight weeks. As a general rule, relapsing fever cannot be checked by "606," an observation that is at variance with the current view. This may be due to a peculiarity on the part of our spirochæte, but a special "606"-fastness was not detectable, as in the mouse the prophylactic and curative effect of the drug was very prompt. In view of its extremely mild course, the necessity for arresting the disease will scarcely ever arise.

Contra-indications for relapsing-fever therapy are only severe heart complications and severe general debility. The aortitis of paralytics does not constitute a contra-indication. Only cases of so-called "galloping paralysis," which take an extremely rapid course right from the start, are not suited for treatment.

The danger of contagion is very slight. We have never isolated our patients and have nevertheless never experienced any untoward infection. It is not even certain whether vermin, lice and bugs, that are generally the source of infection, can communicate the *Spirosoma duttoni*, which is naturally harbored by an African insect, not indigenous in our latitudes. Nevertheless, before the question has been settled beyond dispute, infection is best carried out in rooms free from vermin. The risk of paralytics suffering from malaria passing the disease on by the mediation of anopheles and with the development of epidemic foci, apparently varies greatly with the locality. This problem has been experimentally investigated at Vienna and London by allowing the insects to pass the blood sucked from malarial paralytics into other paralytics. Whereas in Vienna the disease was

not communicated to any patient, in London, twenty-one cases could thus be infected. The epidemiological aspect of this problem must, therefore, be studied for each station separately. Where the climatic conditions and the occurrence of anopheles favor the communication of malaria, treatment with relapsing fever would appear to be most expedient.

In view of the vacillating course of general paralysis and the common occurrence of spontaneous remissions and relapses, the effects of a certain treatment can only be judged by keeping a large number of patients under observation for a long time. Mindful of this fact, we were very conservative in the publication of our findings, and have only recently compiled the figures of the cases treated in 1919-1922 by Steiner at Heidelberg and by me at Munich. We have not included those cases subjected to the therapy in 1923 and 1924, as the period of observation has been too short.

The cases of statistical value under observation in 1919-1922 comprise seventy-six paralytics and seven tabetics. Eighteen of the paralytics had died by the end of 1923, thirty-three lived at home, while twenty-five remained at the clinic. Of the thirty-three non-restricted patients, twenty-five showed favorable remissions, and further two patients partial remissions, while in three the disease remained stationary, progressing in three other cases. One of the twenty-five hospital cases showed a very good remission, one partial remission, nineteen were stationary, while four progressed. To sum up: Twenty-six very good remissions, three partial remissions, twenty-two stationary and seven progressive cases. Eighteen patients died; 34.2 per cent. of the remissions can be regarded as very good. Approximately half the cases that terminated fatally showed remissions up to one year in duration. Apart from the large number of favorable remissions, the small proportion of progressive cases appears worthy of special notice.

The remissions termed "very good" are such where the mental condition of the patients improved to such a degree that they became reëstablished socially and could follow their occupations again. Naturally the degree of improvement attained depended on the stage in which treatment commenced, and accordingly those cases where the paralytic process had not yet given rise to extensive deficiency symptoms responded best. It must be remembered, however, that it is

no easy matter to be sure that a psychical deficiency manifestation is really due to an impairment of the paralytic brain and not merely to transitory conditions such as inattention, stupor, etc. This appears to be the explanation for the fact that complete, or almost complete, psychical recovery after treatment with relapsing fever could be observed in cases where dementia of no inconsiderable extent was present before. The occupations followed by our patients were in part apt to tax their mental powers very considerably. We treated factory owners and merchants who had concerns of their own to conduct, as well as officials and so forth. It was not as though only the capacity for mechanical work was restored. If these patients were examined closely by a specialist, it was found that in the majority certain psychical alterations were still manifest; for example, emotional instability, irritability, abnormal sensitiveness, disposition to hypochondria, bad memory, etc. Such complaints were, however, so slight that associates could scarcely notice them, in no case regarding them as signs of a mental disorder, but at most as symptoms of general "nervousness." Among bodily symptoms that responded to our therapy, articulation and the handwriting deserve special mention, while the pupillary disorders could only seldom be influenced and then only in a very slight measure.

A survey of the results shows that the earlier treatment commenced, the better were the results. Nevertheless, advanced cases, *i.e.*, such where general paralysis had already been manifest for two years, were also to a certain extent favorably influenced in their course. Comparatively incipient expansive cases appeared rather more promising than the much more common forms of simple dementia, but even the latter could be seen to respond, and the majority of our good remissions are recruited from this group.

The time that has elapsed is too short to enable a definite opinion being formed on the average duration of these remissions. It certainly looks as if relapsing fever remissions are of longer duration than those met with in the natural course of the disease, which latter, according to recent figures of Tophoff, relapse again in 73 per cent. of the cases within the first year. The twenty-five remissions we considered very good, at the last control lasted $11\frac{1}{2}$ years in five cases, respectively, 2 to 3 years in fifteen cases and 4 to 5 years in one case. We must add to these figures numerous patients whose condition has

remained stationary, including a large number of general paralytics who were in advanced stages of dementia and in whom the effects of our treatment could only be detected by the arrest of the symptoms. We are justified in assuming that the remissions after treatment with relapsing fever are not only of longer duration; they are, moreover, more numerous and more extensive than those occurring spontaneously. Even the most skeptical must admit that general paralysis responds to treatment in over one-third of the cases.

To what extent permanent remissions or even cures are effected, cannot be judged for the present. The view that general paralysis is an incurable disease under all circumstances cannot be regarded as being correct in principle. We may mention that recently a few cases were published where the anatomical findings favored the assumption that a cure had been effected. Experience has, however, taught us that clinical restitution, be it ever so perfect, is no proof that the underlying anatomical process has been stayed, and conversely it is conceivable that general paralytics have been cured anatomically in spite of the persistence of defects.

Certain conclusions on the internal reactions taking place can be drawn from the spinal fluid findings; at any rate it appears certain that as long as changes in the fluid are observed, the morbid process has not been arrested. Examination of the blood and cerebrospinal fluid demonstrated that the Wassermann reaction very often responded to treatment with relapsing fever. The blood Wassermann was weakened, or it became negative, in 50 per cent., the liquor Wassermann in 61 per cent. of the cases. No strict parallelism between the Wassermann change and the occurrence of remissions could, however, be discovered, although it must be admitted that the reaction was most often affected in patients with remissions, and if these remissions persisted for years, with a few exceptions, the reaction became negative, or almost so. The Sachs-Georgi (flocculation) test responded in the same manner as the Wassermann. The cell-count of the cerebrospinal fluid, which, as mentioned, usually rises during relapsing-fever therapy, sank after some time in remittent cases, sometimes even to normal values. The globulin tests were weakened and the total albumin decreased in quantity, while the curves of the gold and mastix reactions were also distinctly affected.

We treated approximately one-half of the cases in addition with

"606," initially because we thought we could influence thereby the course of the fever, later on, in order to observe whether combined treatment yielded better results. There was nothing to distinguish the cases treated with "606" from those only subjected to relapsing-fever therapy. The number as well as the duration and extent of the remissions coincided almost completely in both series.

It appears probable that the results will be even more favorable if those cases come to treatment that are in such an early stage that only the characteristic changes in the cerebrospinal fluid are observed, but no clinical symptoms. Our aim must be to treat patients in the pre-paralytic stage. No evidence has been produced on the question whether relapsing fever exerts a prophylactic effect, *i.e.*, whether syphilitics who contract the fever before cerebral manifestations have occurred, are protected from general paralysis. A comparison with malaria would appear to negative such an assumption. Syphilitics in the secondary stage who contracted malaria were, nevertheless, seen to suffer from general paralysis (Mühlens and Kirschbaum), and we ourselves have observedluetice patients who caught malaria five and six years before the onset of general paralysis.

Our observations on the influence of relapsing fever on dorsal tabes are too limited to allow of any final deductions being made. Seven cases suffering from severe subjective symptoms, particularly from lancinating pains, were treated; five of them were indubitably seen to respond; the pains disappeared or were relieved very considerably, and locomotor ataxia became less pronounced. A tram conductor who could no longer follow his occupation, owing to the frequent pains, was cured of them completely, and he has now been engaged in his former occupation for three years. These preliminary experimental observations appear to make it worthwhile to carry out the relapsing-fever treatment of tabes on a larger scale.

Relapsing-fever therapy of general paralysis in the hands of other authors has also yielded good results. Sagel treated seventy-two paralytics at the mental hospital of Arnsdorf, near Dresden, since autumn 1921. After deducting the cases still under observation, fifty-five patients remain, of whom twenty-four, *i.e.*, 43.6 per cent., could be discharged fit for work, while remissions occurred in seven further cases. Many of these patients have now been out working for 1 to 1½ years. The last-named worker could also note a direct

influence of the treatment on the blood and spinal fluid findings. Hauptmann, at Freiburg, Werner, at Stuttgart, and Lorento y Patron, in Peru, have expressed favorable opinions on the treatment of general paralysis with relapsing fever. Nine of twelve cases treated in 1919 at the clinic of Weygandt, at Hamburg, according to Kirschbaum and Kaltenbach, suffered remissions that still persisted early in 1923 when the report was published.

As far as we can judge, the results of malaria and relapsing-fever treatment are very evenly balanced. Our figures with the latter show a slightly higher percentage of remissions, but the difference is so small that it lies well within the limits of statistical error.

No definite answer can be given to the question whether relapsing-fever or malaria therapy is the treatment of choice. In their therapeutic effect, as stated, they appear to yield identical results. Malaria has the advantage that it can be checked at a moment's notice with the aid of quinine, while relapsing fever must be allowed to subside by itself. On the other hand, in view of the very mild course of artificial infection, a necessity for prematurely cutting short the fever practically never arises. When malaria has been arrested by quinine, it is possible to resort to re-infection if a renewed deterioration of the patient's condition becomes marked, whereas, as mentioned, re-infection with relapsing fever is impossible even after the lapse of several years. One advantage of relapsing fever is that it is less dangerous for the patient and easier to carry out for the practitioner. In tertian malaria the chills follow each other in close succession. As a general rule, the interval does not remain constant at forty-eight hours; a quotidian type, that is, a tertian duplex, develops, according to observations at Munich and elsewhere, which naturally is apt to exhaust the patient very considerably. The intervals between the peaks of relapsing fever are longer, so that the patient has time to recuperate and the tax on his strength is not so great. In the case of patients with a poor constitution, we therefore prefer treatment with the latter. A danger associated with malarial therapy is that in the case of blood donors coming from the tropics it is not possible to ascertain in advance whether they are suffering from tertian alone or from double infection with *Febris tropica*. Mühlens and Kirschbaum, at Hamburg, have published a case where examination of the blood revealed only tertian plasmodia, while the infection of paralytics

caused *Febris tropica* to develop, with the result that a number of patients succumbed to this infection. Consequently, continuous control of the blood-findings is essential. In the case of relapsing fever, the infectious material consists of microörganisms that have been passing for many years through mice, so that the occurrence of similar accidents is out of the question. The fact that malaria cannot be cultivated in animals makes us dependent on infection from man to man. If it happens that no paralytic whose condition favors malaria treatment is in the clinic, then a break occurs in the passage, and a new blood donor must be sought—not always an easy matter. The passage of relapsing fever in mice is easily kept up and, in consequence, treatment can be interrupted at any time to be resumed again when desired. Great difficulties are further attached to the despatch of malarial virus, as outside the organism the blood remains potent but a short time, whereas the spirosuma of relapsing fever can be sent to any distance in the form of infected mice or as cultures.

We are still entirely in the dark as to the essential cause of the favorable influence of the two diseases on general paralysis. I do not believe that the high temperatures alone are responsible, as occasionally very favorable remissions occur after moderate elevation, while no response is sometimes observed to high temperatures. The fact that two so entirely different diseases as relapsing fever and malaria coincide in their action upon the paralytic process points to a potentialization of the resistant powers of the organism as the factor that is productive of therapeutic success. According to this view, treatment with infectious diseases would represent a very powerful form of non-specific therapy. It must not be forgotten, however, that the spirochætes of relapsing fever cause inflammatory manifestations on the part of the meninges and it might therefore be possible that microörganisms gaining access to the cerebrospinal cavity exert a local action on the general paralytic process. For the present, the solution of the problems involved must remain a matter of conjecture. There is no doubt about the therapeutic response, but we are unable to elucidate its underlying cause. As scientists we remain dissatisfied, but as practitioners, we can be well content with the fact that we are in a position to restore mental and bodily vigor to a certain proportion of general paralytics that were thought to be already on the brink.

THE MOTIONS OF THE LARGER JOINTS *

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A SURGEON once wrote to ask me what another surgeon meant when he said that after a certain operation "he dressed the shoulder in the elevated position." From what I knew of the practice of the surgeon in question, I was quite sure he meant that he dressed the shoulder in abduction and external rotation; and I so replied to my correspondent. But it is evident that one cannot always interpret correctly inaccurate statements which too often, alas, are due to inaccurate thinking. This general state of muddle-headedness is evinced by a great many descriptions of joint lesions. The expressions "with the shoulder in the elevated position," "with the knee abducted," "with the foot rotated out," "with the arm (or the leg) flexed," are all of them comprehensible only with the aid of an active imagination. For instance "with the knee abducted" is an expression frequently used when the writer means "with the hip in the abducted position," or "with the lower extremity abducted at the hip"; there is no such motion as abduction or adduction in a normal knee. Still more exasperating are expressions which have a pseudo-accurate appearance, such as "with the leg bent fifteen degrees," or "there was ankylosis of thirty degrees."

It has seemed worth while, therefore, to attempt to systematize the nomenclature of the movements of the larger joints.

It is well to begin by recalling what is known as the "anatomical position" of the body: The body erect, the upper limbs hanging by the sides of the trunk, with the palms of the hands forward, and the lower limbs side by side with the toes pointing forward. It is advisable also to note the distinction between the terms *arm* and *forearm*,

* This paper was prepared while the writer was at the front during the German War (1918). Its publication has awaited an opportunity for procuring adequate illustrations. (The drawings are by Mr. E. F. Faber.) Meanwhile, other contributions of a similar nature have appeared (ROSÉN, *Journ. Bone and Joint Surg.*, 1922, xx, 570; SILVER, *ibid.*, 1923, xxi, 569). This shows that the subject is considered worthy of study.

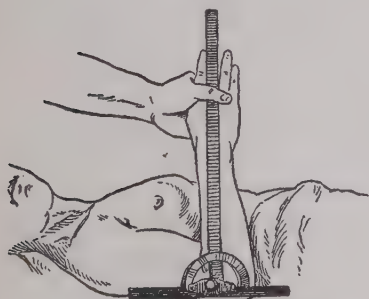
thigh and leg. Next it is well to adopt a definite nomenclature to designate the *range of motion*: It is a mathematical axiom that the sum of two right angles is a straight line, or 180 degrees. There are very few joints (no normal joints, I believe) that have a range of motion greater than 180 degrees. It is sufficiently simple, then, to record joint motions as ranging from the least possible angle that the segments of the limb can make with each other up to the straight position which is recorded as 180 degrees. Thus, the elbow when straight is at an angle of 180 degrees; when flexed to a right angle it is at 90 degrees; when flexed not as far as a right angle it is at, say, 135 degrees, and when flexed almost fully it is at an angle of 45 degrees or less. (Fig. 1.) A *goniometer* is an apparatus used for measuring joint

FIG. 1.



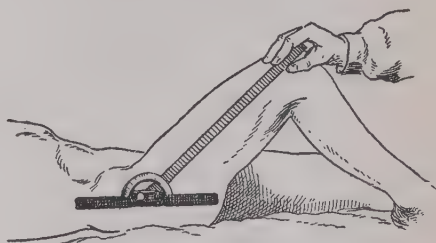
A straight line is 180°; this corresponds to the fully extended position of a joint (as the elbow); flexion to a right angle is 90° flexion; flexion less than this (135°) and more than this (45°) are shown in the diagram.

FIG. 2.



Goniometer indicates elbow flexion to 90°.

FIG. 3.



Goniometer indicates flexion of hip to 135°.

motions: Its centre of motion is applied at the axis of the joint, and one of its limbs is applied to each segment of the limb forming the joint whose motions are to be recorded (Figs. 2, 3). Records made by the aid of the goniometer certainly are not unerringly accurate, but if made at intervals by the same examiner the error in appreciating increase or decrease or stationary condition of the joint motions under investigation is much less than when the range of motion is measured by the eye alone.

In describing movements it is desirable to have names for the three planes in which motion may occur. In anatomy one speaks of the *sagittal* (or antero-posterior vertical) plane; of the *frontal* (or

coronal or transverse vertical) plane; and of the *transverse* (or transverse horizontal or transverse antero-posterior) plane. The body being considered always as in the anatomical position (whether erect or recumbent), that is, all the limbs being in the frontal plane:

Flexion and extension are those motions which occur in the sagittal (antero-posterior vertical) plane.

Adduction and abduction are those motions which occur in the frontal (transverse vertical) plane.

Inversion and eversion are those motions which occur in the transverse (transverse horizontal) plane. As will be seen, the only movements of this kind are very limited in extent and occur in the tarsal joints.

Rotation is that movement of a joint which occurs in the long axis of the distal segment of the limb forming the joint, no matter in which of the three planes the segment in question may happen to be moving: Thus one speaks of rotation of the humerus on the scapula, not the reverse; of rotation of the femur on the pelvis, not of rotation of the pelvis on the femur; and rotation may occur whether the joint is flexed or extended, adducted or abducted, though its range usually is greater in one position than another.

Circumduction is that movement of a joint which takes place consecutively in several planes: It combines the motions of *flexion, abduction, extension, and adduction, or vice versa*.

Flexion and Extension.—These are the only motions in hinge joints—elbow, knee, and ankle (tibio-astragalar); also in the interphalangeal joints. They occur also, as do other motions (adduction and abduction, rotation and circumduction), in the shoulder, carpal, hip, and tarsal joints.

Adduction and abduction occur in the shoulder, wrist, hip, and subastragalar joints; also in the metacarpo- and metatarso-phalangeal joints.

Rotation occurs in the shoulder, radio-humeral, hip, and mid-tarsal joints. It may be more extensive in some positions of a joint than in others; thus it is present to a slight degree in the knee-joint when this is flexed to a right angle and it is more free in the flexed than in the extended hip. Rotation is recorded as *inward or outward* (internal or external) according as it turns the anatomical front of the limb toward or away from the median line of the body.

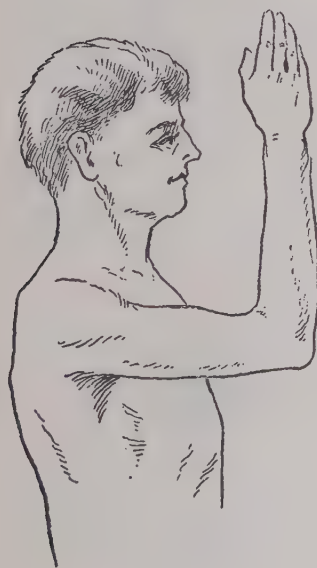
Circumduction is possible in the shoulder, carpal, hip, and tarsal joints; also in the metacarpo- and metatarso-phalangeal joints. It may be *inward* (internal) or *outward* (external): In the former the movement is "clockwise" (to the examiner) on the patient's right side, but "contra-clockwise" on the left. Outward circumduction is the reverse. The segment of the limb which is moved (arm, thigh) delimits a cone whose apex is the joint (shoulder, hip) concerned.

MOVEMENTS OF THE SHOULDER-JOINT

It is important to eliminate the movements which occur between the scapula and the trunk, since they give a false idea of the range of motion possible between the humerus and scapula.

(1) *Flexion and extension*, or motion forward or backward in

FIG. 4.



Flexion of shoulder to 90° , the normal limit.

FIG. 5.



Extension of shoulder to 250° (70° back of the "anatomical position" of 180°).

the sagittal plane, have a range of about 160 degrees. Considering the anatomical position, with the arm by the side, as 180 degrees, flexion normally is possible almost to 90 degrees and extension about to 250 degrees (Figs. 4 and 5). In recording lesions of the shoulder-

joint which limit these movements, the expression should be "flexion limited to 135 degrees," "extension only to 200 degrees," or more simply, "Fl. Ext. 135-200°." (Figs. 6 and 7.)

(2) *Adduction and Abduction*.—In the anatomical position the

FIG. 6.



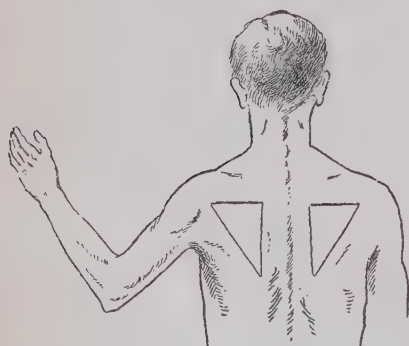
Flexion of shoulder to 135°.

FIG. 7.



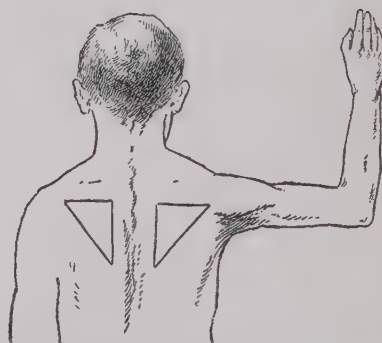
Extension of shoulder to 200°.

FIG. 8.



Abduction of shoulder to 45°.

FIG. 9.



Abduction of shoulder to 90°.

arm, hanging by the side, makes no angle with the sagittal plane; as the arm is carried away from the side (*abduction*) the angle increases up to 90 degrees, which is the normal limit (Figs. 8 and 9). Further abduction is secured only by rotation of the scapula on the chest, and in determining the range of motion in the shoulder the scapula should

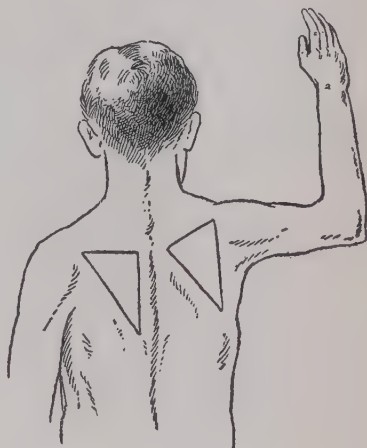
be fixed (Figs. 10 and 11). *Adduction* of the shoulder is not possible in the anatomical position, but if the shoulder is flexed until the elbow clears the side of the chest, adduction becomes possible up to perhaps an angle of 45 degrees; often it is less than this, only perhaps

FIG. 10.



Elevation of arm above horizontal is secured only by rotation of scapula on chest.

FIG. 11.



If ankylosis of shoulder exists, abduction even to 90° is secured only by rotation of scapula.

an angle of 30 degrees from its original position in the sagittal plane. It is seldom that the elbow can be brought beyond the midline of the body without some motion between the scapula and chest (Fig. 12).

(3) *Rotation*.—With the arm in the anatomical position, if the elbow be flexed to a right angle the forearm will lie approximately in the sagittal plane. The bicipital groove looking directly forward in this position, the shoulder-joint is in a neutral position as regards rotation: That is to say, it is neither in external nor in internal rotation.

If now, with the forearm flexed, the hand is moved out transversely away from the body, with the elbow held close to the chest, the forearm moves in the transverse horizontal plane while the humerus remains vertical: This produces rotation (outward) at the shoulder-joint. Unless the elbow is kept flexed at a right angle and with the

FIG. 12.



Adduction of shoulder.

forearm in full supination, it is very difficult to differentiate between rotation in the forearm (radio-ulnar and radio-humeral joints) and that in the shoulder-joint. In outward rotation of the shoulder the

FIG. 13.

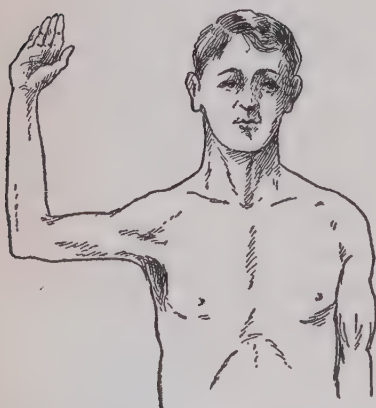


External rotation of left shoulder to 90°; of right shoulder to 45°.

forearm normally will be arrested when it reaches the frontal plane, that is to say, when rotation outward of 90 degrees has occurred at the shoulder (Fig. 13, left shoulder). Any limitation of this range of normal outward rotation should be recorded as "outward rotation only to 30

degrees," or "external rotation limited at 60 degrees," etc. (Fig. 13, right shoulder.) Fig. 14 shows outward rotation to 90 degrees combined with abduction to 90 degrees. *Inward rotation* is still

FIG. 14.



External rotation of shoulder with abduction to 90°.

FIG. 15.



Internal rotation of shoulder with abduction to 90°.

more difficult to recognize unless the elbow is flexed and the forearm kept fully supinated. In this position, with the humerus by the side of the body, inward rotation is limited only when the forearm is arrested by contact with the body. But if the shoulder is

either flexed or abducted, so that the elbow clears the body, then internal rotation becomes more free, but it seldom exceeds 90 degrees (Fig. 15), and it is difficult to exclude some movement between the scapula and the chest.

(4) *Circumduction*.—This is a combination of flexion, extension, abduction, and adduction. *Internal circumduction* is that where the movement is clockwise on the patient's right side, but contra-clockwise on the left. *External circumduction* is the reverse. In either case the elbow moves through a circle or ellipse, the arm delimiting a cone whose apex is at the shoulder-joint.

MOVEMENTS OF THE ELBOW-JOINT

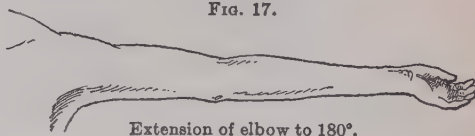
(1) *Flexion and Extension*.—The range of normal motion is from 30 or 35 degrees of flexion (Fig. 16) up to full extension (180

FIG. 16.



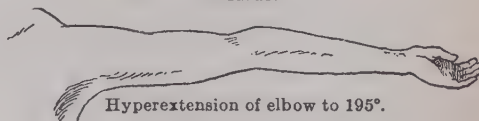
Flexion of elbow to 30°.

FIG. 17.



Extension of elbow to 180°.

FIG. 18.



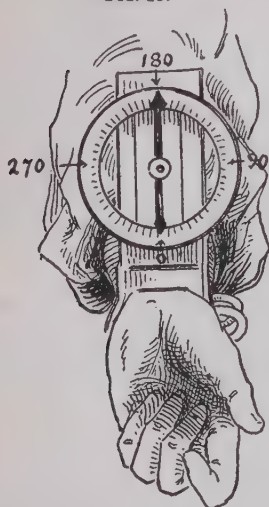
Hyperextension of elbow to 195°.

degrees) (Fig. 17). In many individuals, especially children and women, a certain amount of *hyperextension* is possible. This rarely passes beyond 190 or 195 degrees (Fig. 18).

Rotation of the forearm, which, properly speaking, occurs not in the elbow-joint but in the radio-ulnar joints (upper and lower), may be included here for the sake of completeness, and because its integrity depends upon freedom of motion between the radial head and the capitulum of the humerus. Taking the position of supination as the normal anatomical position this may be considered an angle of 180 degrees compared with the normal limit of pronation, which is about 15 or 20 degrees, though it is often more limited, in those whose forearms are muscle-bound by over-development. In some cases (particularly women and children) the range of supination is greater than the average, up to 200 degrees or even more. The use of an instru-

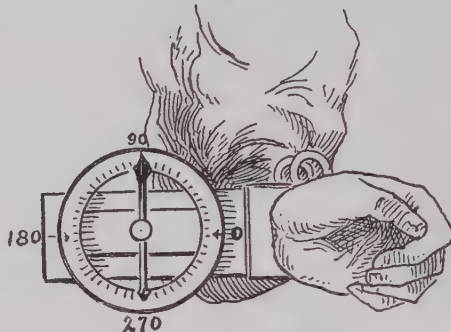
ment such as shown in Figs. 19 and 20 gives a fairly accurate record of the range of rotation.

FIG. 19.



Forearm in full supination, reckoned as 180° by indicator of pronometer.

FIG. 20.



Forearm pronated to 90°.

MOVEMENTS OF THE WRIST-JOINT AND CARPUS

The motions which occur in the radio-carpal joint (properly speaking the wrist-joint) are flexion and extension, adduction and abduction, and circumduction, but no rotation.

FIG. 21a.



Flexion of wrist to 90°.

FIG. 21b.



Hyperextension of wrist to 250° ±.

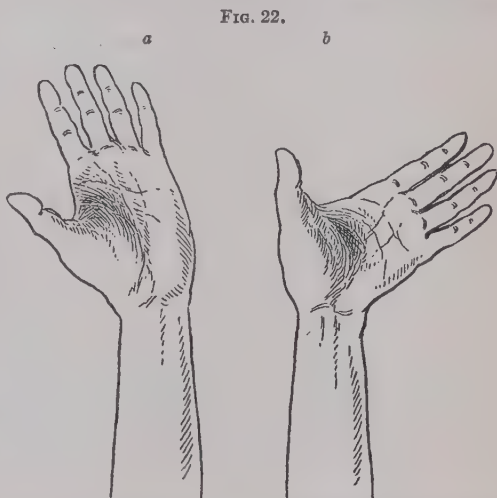
(1) *Flexion and Extension*.—The anatomical position of extension being regarded as a straight line (180 degrees), flexion normally occurs almost to 90 degrees, and extension (hyperextension) not quite so far, perhaps to 250 degrees. (Figs. 21a and b.)

(2) *Adduction and Abduction*.—Adduction (ulnar deviation) is more extensive than abduction (radial deviation), but rarely exceeds 45 degrees. Abduction usually is limited at 10 to 15 degrees, though an apparently greater range of abduction is possible when it is combined with hyperextension (Figs. 22a and b).

(3) *Circumduction* takes place up to the limits possible for its component movements. It must not be confused with rotation in the forearm.

If the mid-carpal joint be considered as one in its movements with the radio-carpal

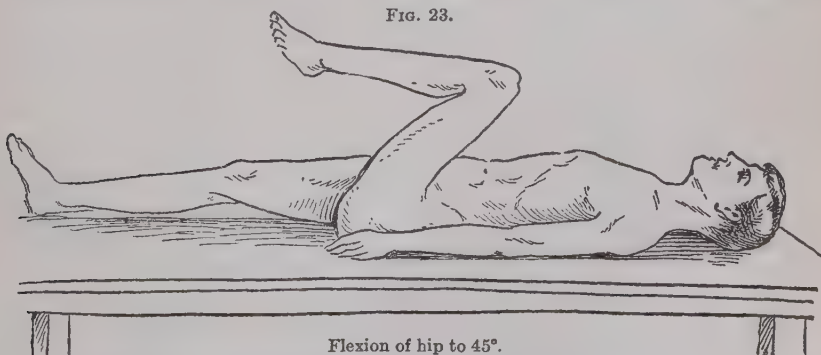
joint, all the motions named above become more free; according to some authorities a little rotation may occur in the mid-carpal joint.



Abduction of wrist to 15° (a). Adduction of wrist to 45° (b).

MOVEMENTS OF THE HIP-JOINT

(1) *Flexion and Extension*.—Flexion is limited by contact of the soft parts, usually at an angle varying from 30 to 45 degrees.

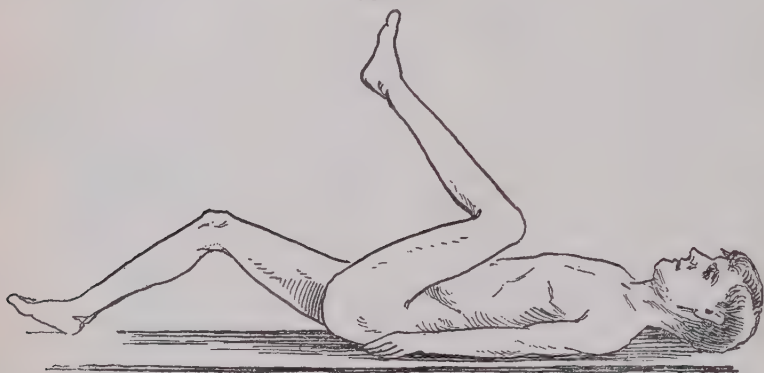


Flexion of hip to 45°.

It is important to maintain the other hip in full extension; otherwise attempts at continued flexion of the hip under examination will cause flexion of the pelvis on the spine, or even of the spine, and give an

erroneous idea of the extent of flexion actually present. (Figs. 23 and 24.) *Hyperextension* of the hip normally occurs to an angle of 190 or 200 degrees (that is, 10 to 20 degrees beyond full extension) ; here again it becomes important to exclude compensatory move-

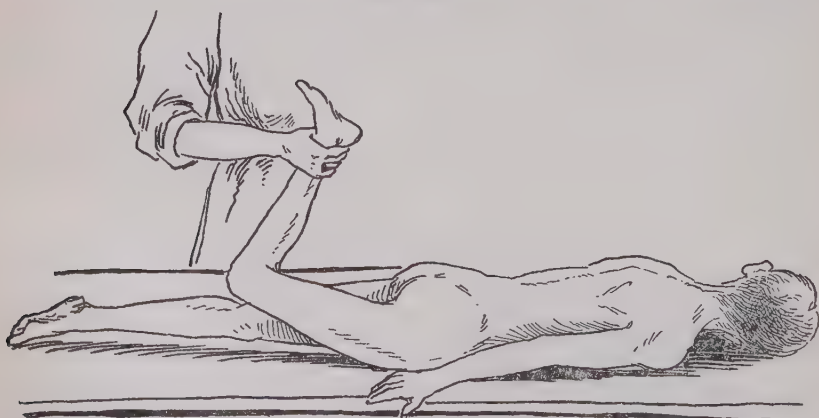
FIG. 24.



Apparent flexion of hip to normal limit, but secured only by flexing the pelvis on the lumbar spine, as indicated by the other limb rising from the table.

ments in the pelvis or lumbar spine: The patient should be examined prone, and the opposite thigh should be kept on the table, while attempts are made to hyperextend the hip under examination by

FIG. 25.



Hyperextension of hip to 190° or 200° (10° or 20° extension beyond the neutral position of 180°).

means of the leg with the knee flexed (Fig. 25). Or the patient may lie supine, with both lower extremities hanging over the foot of the table; in this position, even with all possible compensatory

hyperextension in the pelvis and lumbar spine, loss of hyperextension or even of normal extension in the diseased hip becomes readily apparent (Fig. 26).

(2) *Adduction and Abduction*.—These motions must be separately studied (a) when the hip is in full extension, and (b) when it is in flexion at a right angle or thereabouts.

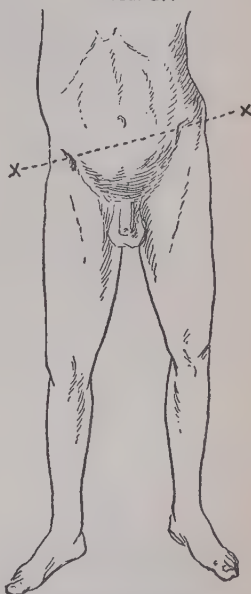
(a) In full extension, adduction requires a corresponding abduc-

FIG. 26.



Loss of normal extension in the left hip (as from psoas abscess) demonstrated by hanging both lower extremities over the end of the table. The normal (right) hip goes into hyperextension.

FIG. 27.



Adduction of left hip to 35°.

tion of the other thigh; normally adduction occurs about to an angle of 35 degrees (Fig. 27). *Abduction* usually is limited at an angle of 45 to 60 degrees (Fig. 28).

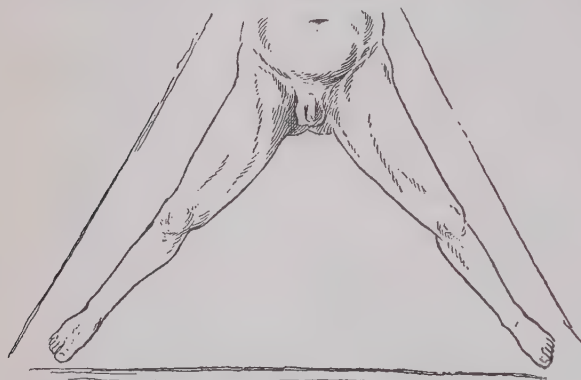
(b) In *flexion*, adduction is possible to 45 degrees, and *abduction* nearly to a right angle (Figs. 29 and 30). Note that in Fig. 30 the hip is not only abducted but also externally rotated. This position will be discussed later.

(3) *Rotation* at the hip also varies with the position of the limb. In either case the patient should be examined recumbent.

(a) In *extension*, rotation takes place approximately through an arc of 90 degrees, in internal rotation the patella being turned toward

the other knee, and in external rotation being turned outward. The readings are to be made in degrees from the sagittal plane, as at the shoulder. By examining the patient in the prone position with the knee flexed, and using the leg (which then is vertical) as a

FIG. 28.



Abduction of both hips to their normal limit (each at angle of $45^\circ \pm$).

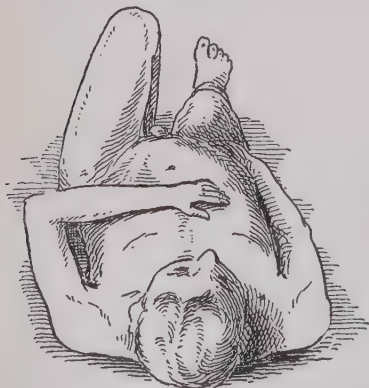
In this position also it must be remembered that the angle through which rotation occurs is to be recorded *from* the sagittal plane, not *toward* the sagittal plane. Complementary angles being equal, the

guide, the range of rotation can be very easily determined (Figs. 31 and 32).

(b) In *flexion* with the knee also flexed, and the patient supine, rotation has a much wider range, perhaps 135° (Figs.

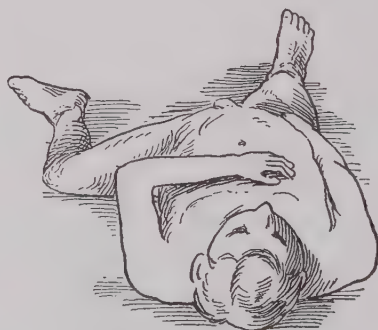
33 and 34). In

FIG. 29.



Adduction of the flexed (left) hip.

FIG. 30.

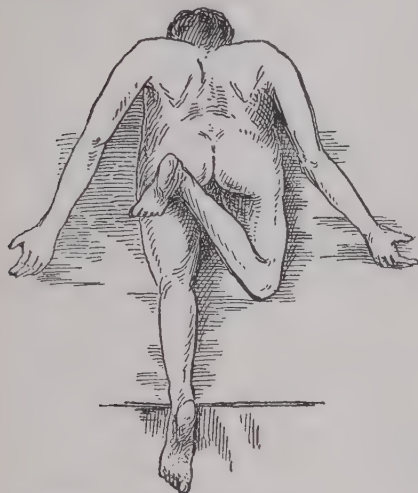


Abduction of the flexed (left) hip.

reading DBC (Fig. 33) is much more easily made between the leg (BD) lying in the horizontal plane, and the position from which the leg was raised (BC) than between the imaginary prolongation of the line DB to E , and the normal position ABC . The angle DBC is equal to the angle ABE .

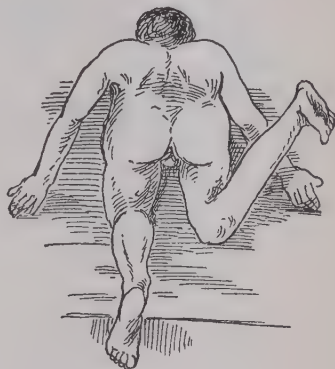
It must further be noted that rotation outward is present in the hip which has been flexed and then fully abducted, as in Fig. 30,

FIG. 31.



External rotation (60°) of the right hip.

FIG. 32.



Internal rotation (30°) of the right hip.

A° FIG. 33.

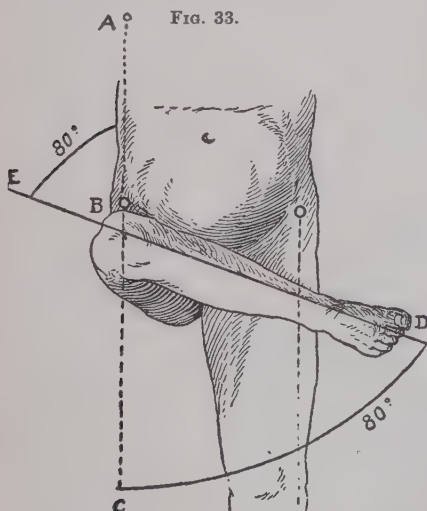
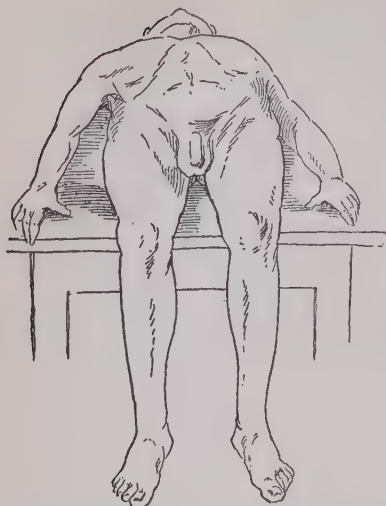
External rotation of flexed (right) hip to 80°
(normal limit about 90°).

FIG. 34.

Internal rotation of flexed (right) hip to 210°
(30° beyond sagittal plane).

since the patella looks outward. If the hip is merely abducted without being flexed, and the patella continues to look forward (as in Fig. 28) the range of abduction is much less (about 45 degrees).

Fig. 35.



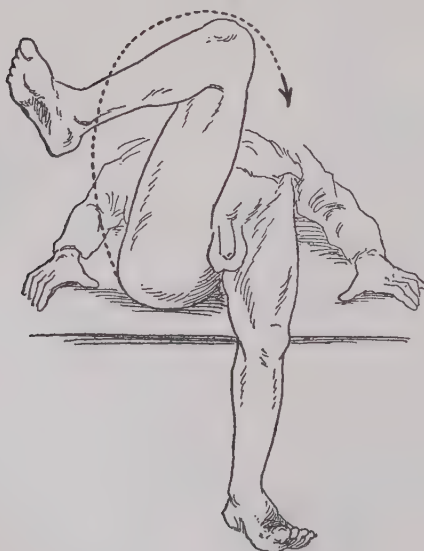
Both knees flexed and hanging vertical: If hip were fixed in ankylosis in internal rotation, the leg would deviate away from its fellow; if in external rotation the reverse would be noted.

Fig. 36.



External circumduction of right hip.

Fig. 37.



Internal circumduction of right hip.

The absence of rotation can be ascertained by flexing the knee, when, if the patient is lying on his back, the leg will hang vertically if rotation is absent (Fig. 35). If in this position the leg instead of hanging vertical deviates outward, it indicates that the hip is ankylosed in internal rotation; if the leg deviates inward, the hip is ankylosed in external rotation.

A curious phenomenon takes place if in the flexed and abducted hip (which is also in outward rotation) (Fig. 30), the outward rotation is abolished without abolishing the abduction: The limb now at once assumes the position shown in Fig. 28 where only abduction is present, and the flexion (so-called) has been abolished. But if it be remembered that flexion was defined as a motion occurring in the sagittal plane it is seen at once that in reality no true flexion is present in the limb as shown in Fig. 30, but only abduction and external rotation, though it is customary to describe the position as one of flexion-abduction (the "primary position" in reduction of congenital dislocations of the hip).

(4) *Circumduction* at the hip scarcely requires comment. It is *external* when the thigh from the position of extension first passes into adduction, then into flexion, next into abduction, and finally again returns to extension (Fig. 36). It is *internal* when abduction and flexion precede adduction and final return of extension (Fig. 37).

MOVEMENTS OF THE KNEE-JOINT

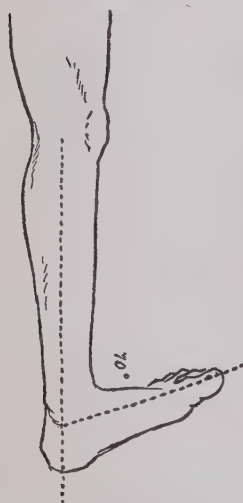
(1) *Flexion and Extension*.—Flexion usually is arrested by contact of the soft parts about at an angle of 45 or 30 degrees; in muscle-bound limbs it is arrested rather by tension on the extensor apparatus. The position of extension is 180 degrees, and normally no hyperextension is present.

(2) *Rotation* becomes possible to a very limited degree only when the knee is flexed to a right angle. If examination be made with the patient recumbent, and with the hip as well as the knee flexed to a right angle, then *external rotation* and *internal rotation* both may be measured by the angle made by the foot with the sagittal plane; but it is very easy to be deceived by movements of eversion or inversion in the foot itself.

MOVEMENTS OF THE ANKLE-JOINT

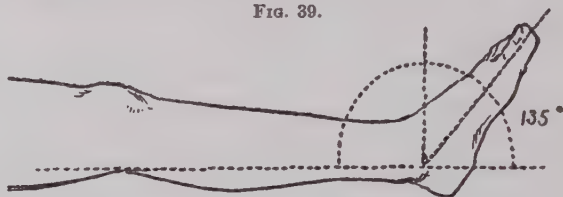
Flexion and Extension.—The normal neutral position is at 90 degrees. Flexion (dorsi-flexion is more explicit) occurs normally about to 70 degrees, being arrested largely by tension on the tendo

FIG. 38.



Flexion (dorsi-flexion) of ankle to 70°.

FIG. 39.



Extension (plantar flexion) of ankle to 135°.

achillis, while extension (plantar flexion) is limited around 145 to 150 degrees by tension on the anterior structures (Figs. 38 and 39). Other movements take place not in the ankle-joint proper (tibio-tarsal joint) but in the tarsal joints.

MOVEMENTS OF THE TARSAJ JOINTS

(1) *Flexion and extension* occur to a limited degree in the mid-tarsal joint (that between the astragalus and calcis posteriorly, and the scaphoid and cuboid anteriorly). In cases with ankylosis of the ankle-joint motion at the mid-tarsal joint largely compensates for the loss of movement in the ankle.

(2) *Adduction and abduction*, which I have defined as movements in the frontal plane, occur to a slight degree in the subastragalar joint (which includes both the astragalo-calcanean and the astragalo-scaphoid joints): In *adduction* the plantar surface of the heel tends to face inward, while in *abduction* it faces outward.

(3) *Supination and pronation*, which are functions of *rotation*, occur chiefly in the mid-tarsal joint: In the former the sole turns inward (varus position); strictly speaking this would be external rotation, as the distal part of the foot moves upon the proximal in such a way that the anterior anatomical surface turns away from the median line. In pronation the sole turns outward (valgus position, internal rotation). The terms "internal" and "external" rotation are so easily misunderstood in connection with movements of the foot that it is not advisable to employ them at all. They should

be substituted by the terms "pronation" and "supination" (Figs. 40 and 41).

(4) *Inversion and Eversion*.—Theoretically these are those movements made by the foot in the transverse horizontal plane; the axis of motion lies in the sagittal plane a little anterior to the tibia: In inversion the toes point toward the other foot, and the heels are apart; in eversion the heels are together and the toes apart. These motions, very slight in extent, occur in the subastragalar and mid-tarsal joints simultaneously. Great care must be taken to ex-

FIG. 40.

Pronation of the foot
(valgus position).

FIG. 41.

Supination of the foot
(varus position).

clude rotation of the whole lower extremity at the hip, in estimating the degree of inversion or eversion possible in the tarsal joints. Practically, no such movements occur: *Inversion*, as defined above, is inseparable from supination; *eversion* converts the foot into a rigid lever, transferring the motion to an attempt at external rotation of the astragalus in the tibio-fibular mortise (ASHHURST and BROMER, "Classification and Mechanism of Fractures of the Leg Bones Involving the Ankle," *Archives of Surgery*, 1922, iv, 99).

Electrotherapeutics and Physiotherapy

THE CLINICAL ACTION OF DIATHERMY

By FREDERIC DeKRAFT, M.D.

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HIGH-FREQUENCY machines, as supplied to medical men to-day, have become so perfected that it is possible to subject them to long hours of arduous work, with a minimum of mechanical attention; and the art of their use has reached such a degree of perfection that we are able to gauge the heat effect from an almost imperceptible warmth, as applied to the most delicate structures of the body, to a desiccating heat that will quickly and bloodlessly cut into tissues as exemplified in the acusector.

The application of heat in some form to the alleviation of human ills probably began with the dawn of human intelligence. The use of poultices in the treatment of inflammatory processes, such as pneumonia, myalgias, boils, rheumatic arthritis, etc., is old. The use of the sun's rays and the application of hot water date back to remote antiquity.

But all these methods were useful to apply heat from without only. It remained for diathermy (that one of our most interesting of modern weapons against deranged functional activities) to enable us to generate heat in the tissues themselves. Among the important links in the chain leading to this result were the discovery of the Leyden jar by von Kleist in 1745, and of electromagnetic induction by Oersted in 1821, and the work of Faraday, the studies of Æpinus and Cavendish, and the description of the static induced current by William J. Morton in 1881. The works of Tesla and d'Arsonval, of von Preyss, von Zeynek and many others, helped to lay the foundation of one of our most interesting modern weapons against deranged functional activities of the various parts of the body. Diathermy is the only means which enables us to simulate fever heat, for diathermic heat is generated in the tissues themselves. The passage of the high-frequency current through the tissues produces a peculiar

molecular disturbance, a mechanical agitation of extreme minuteness which results in heat. This heat is produced without any evidence of chemical, of electrolytic decomposition. This is made possible by the inconceivably rapid alternation of this oscillatory current. In other words, there is no polarity effect.

It is because of this entire absence of polarity that we are enabled to introduce currents of electricity into the living body in sufficient volume to produce thermometric, demonstrable heating effects in the tissues and blood of patients, without destructive action on nerve-fibre or delicate cellular structure. This warming is different from that obtained by any other method. We have it in our power to introduce it in any measurable quantity throughout the entire body. Or we may concentrate its action to any part or organ, either on the surface or at any depth. In this interior heat every cell participates, centres of heat are formed in millions of cells. A heat which is very slowly dissipated. The deeper the seat of the cell, the more slowly it loses its stored heat.

By a reflex effect, an addition of heat beyond the normal stimulates all those functions which favor the emanation of heat. The capillaries of the skin and mucous membranes of the nose, throat, and bronchi become widely dilated. Great quantities of blood are drawn to the surface of the body for cooling purposes. Much of this blood, thus drawn to the surface, is taken from the splanchnic circle. Thus the heat passes off by the skin and mucous membranes.

The amount of this heat emanating from the body is governed by the temperature of the surrounding air and by the amount of body covering. The temperature of the surface of the body is lower than that of the blood. An extensive peripheral hyperæmia makes possible greater losses of heat. The watery emanation from skin and mucous membranes of the air passages, and the secretion of sweat enhances the dissipation of vapor. The rapidity of the respiratory excursions increases the activity possible by the mucous membranes.

This automatic regulation of the body enables us to tolerate an addition of heat up to a definite point without changing our temperature. A strictly local application to a joint will not markedly affect the general heat capacity of the body. Large electrodes and heavy currents and a longer duration of the séance will exercise all the powers of defense which we have detailed. But let us go beyond

this stated definite point, and a rise of the temperature of the blood of the entire body is inevitable.

A relatively small amount of diathermic current, applied to a little animal, like the guinea-pig, will raise the temperature of its body to the point where paralysis of the heat-regulating apparatus occurs. The reason is simple. The acceleration of the blood stream at the point of contact of the electrodes is greatly intensified. In a relatively short time the entire volume of blood in the animal is heated to the danger point. The greater the strength and concentration of the current, the more rapid the lethal effect. Diathermic currents have a definite influence on the sympathetic and autonomous nervous system.

There is no organ so deeply seated that it cannot be reached by the diathermic heat. By it all gland secretions can be augmented. The functions of the sweat glands, of the liver, the pancreas, the gonads, the thyroid, the kidneys, the stomach, of all the endocrines, may be stimulated. With suitable application of the electrodes, proper dosage and duration, we have it in our power to induce an active arterial hyperæmia anywhere. By the use of large electrodes applied to the trunk of the body and by more general methods of application, such as the multiple electrode method, we may cause great quantities of the blood to rush to the surface of the body. This marked activity of the arterial circulation relieves venous congestion wherever present. Anæmia of the splanchnic area ensues.

When the action of the diathermic current has subsided and the blood stream is again in normal channels, freshly oxygenated arterial blood enters abundantly into the area previously anæmic and venously congested. The parts are placed in a better state of nutrition and in a better attitude of defense against the invasion of toxins and bacterial colonies. Relief from passive venous congestion restores, in great measure, the activity of the liver, pancreas, kidneys as well as the natural secretion of the intestinal mucous membranes.

Because of the very deep and extensive effects of these currents when applied to a large surface of the body, or when the entire body is subjected to its warming influence, it is well to bear in mind what follows: That the ensuing anæmia in the splanchnic area and the removal of stagnant venous blood from the abdominal organs may throw much detritus and poisonous material into the general circula-

tion. Should this occur an acute toxæmia will follow. This may result in fainting or a more or less serious collapse attended with the passing off of foul gases from mouth and rectum and other alarming symptoms.

It is always advisable to take special precautions when administering heavy currents. The bowels should be thoroughly emptied. Watch the action of the skin, for if the sweat glands fail to respond, additional work would then be thrown on the kidneys. The application of heavy currents by means of large electrodes or the auto-condensation couch will usually raise the frequency of the pulse, and may cause a rise of blood-pressure, especially in patients suffering from auto-toxæmia.

An excessive quantity of current for too long a time to a cirrhotic liver will result in over-burdening the capacity of the arterial and venous circulation of this organ. This will result in an increase of accumulation of fluid in the peritoneal cavity. A safe rule to follow (when aiming to increase the functional activity of an organ or a part) is to use mild currents of somewhat longer duration. This applies also if we wish to affect deeply seated organs, like the stomach. Here we achieve our object more quickly with milder currents of longer duration than with heavy currents of too great concentration. The latter rouse the reflexes quickly, and a rapid afflux of blood to the overlying structures—the muscles and skin—occurs, carrying off a large part of the diathermic heat.

The degree to which an active arterial hyperæmia may be of benefit to the patient is dependent upon the nature of the pathological condition. The application of too much current to an arteriosclerotic limb will induce an influx of an excessive quantity of arterial blood. This will greatly overtax the venous system of the part. The result will be intensification of the pain from which the patient is suffering as well as other disagreeable consequences. This is the more likely to happen if the current is applied lengthwise to the limb.

A plan likely to yield good results is to apply the electrodes to the sides of the limb in different sections. Mild currents, applied in this manner, have afforded relief from pain, improved the nutrition, and warmth of the limb, not temporarily, but permanently. Mild currents applied from different points on the outside of the body (a cross-fire effect) achieve effects better than heavy currents.

Diathermy applied to an organ of the body induces stimulation of cell function and an increase in its chemistry. This means an increased vital function which is based on improved metabolism. The active arterial hyperæmia, which follows, brings more nourishment to the cells, adding to their working ability. Improvement in the arterial circulation is accompanied by removal of venous stasis and increased lymphatic flow. This causes removal of waste products. In toxic states of the system, we obtain hereby a detoxication of the part. The removal, in this way, of waste products relieves irritability in the autonomous nervous system, thus removing one of the causes of arterial spasm.

Diathermic currents have marked analgesic properties. This analgesic effect is due to the great rapidity of the oscillations, to the desiccating influence, to the marked arterial hyperæmia which it induces and to the decongesting influence which it is capable of exerting in proper doses. The marked arterial hyperæmia tends to soften scar tissue. The injection of the capillaries with a greater abundance of arterial blood improves the nutrition, and thereby changes slowly organized structure into one of a higher order of vitality.

Diathermic currents applied in a more or less general way, such as the condenser couch, have distinct quieting effect. The patient on the couch becomes fully relaxed and frequently falls asleep. Fibrillary contractions of muscular fibre, in the very early stage of peripheral paralysis, can be arrested by judicious local application of diathermic currents. In those disorders of the nervous system attended by wasting of muscles, the early use of these currents will do much in arresting and (where possible) in removing muscular atrophy; as well as restoring the highest possible degree of function. Bacteria are capable of living only within certain well-defined temperature limits. Their capacity for reproduction is damaged when this limit is exceeded. The temperature limit at which different kinds of bacteria cease to exist varies greatly. In some it is only a few degrees above the normal temperature of the human body.

Diathermy is a certain means of raising the temperature of a part to any desired degree. Where the location of the pathological process permits, we may raise it to the point where certain bacteria die. The gonococcus may thus be killed. If, however, the pathological process, initiated by the gonococcal invasion, is seated in very vascular

structures, like the fallopian tubes, we may find it difficult to raise the local temperature to the required degree. It is possible, however, to raise the temperature of the pelvic organs and of the blood to 104 degrees Fahrenheit by using the large electrodes, one over the sacral region and the other over the abdomen just above the symphysis pubis.

Dr. Ludwig Tutscheck reports his experience with diathermy in inflammatory conditions of the pelvic organs in women, in the *München. med. Wochenschrift* (Sept. 9, 1921). During three years, 300 patients were treated at the gynecological clinic of the University in Munich. All other conservative methods had failed; whereas the results with diathermy were satisfactory throughout. He found this treatment valuable in inflammatory swellings of the adnexa in subacute and chronic stages of parametritis.

Here is the method which yielded best results. He placed a suitable metal electrode either in the vagina or rectum. A metal plate was placed over the abdomen or back, opposite the position of the internal electrode. He used relatively small electrodes with the object of securing the greatest possible concentration of the heat. When the internal electrode was in the vagina, he placed a thermometer in the rectum. When in the rectum, then the thermometer was placed in the vagina. A temperature of 111° F. was reached in this manner. The duration of the treatment was at first fifteen minutes, and the current strength one ampere. This was gradually increased to one hour in duration, and 250 amperes in strength.

The active electrode was always placed in contact with the seat of the inflammatory process. In posterior and lateral parametritis the active electrode was placed in the rectum in direct proximity to the infiltration. In tumors of the adnexa, it was placed either in the vagina or rectum, according to the site of the tumor.

In five cases the objective evidences of the diseased process disappeared in a very short time, the patients being relieved of pain and other discomforts. In other cases, there was only a moderate diminution of the swelling, but the patients were relieved from pain and saved from operations otherwise necessary. In a third class of cases, no visible results were obtained after thirty or forty treatments. Here there were small hard tumors, little movable, the result of old inflammatory adhesions. Subsequent operations showed the hard

tumors, or tubo-ovarian swellings containing abscesses, had become firmly imbedded in old inflammatory adhesions.

The present writer employed a similar technic in cases of old mixed infections of the pelvic organs, and with most gratifying results. One case in particular may be cited. As the result of repeated abortions, there remained considerable enlargement of the uterus, swelling of the adnexa, a chronic discharge, foul-smelling and very irritating, from the uterine canal, and constant pain. Malignancy was suspected and many methods of treatment had been vainly tried by various medical men. Forty applications of diathermy removed all local evidence of disease; all pain and discomfort.

With the employment of a carefully studied technic and suitable concentration of the heat effect, it is possible with diathermy to eradicate old foci of infection. This has been accomplished in many cases of gonococcal arthritis. If any pain and stiffness still persist, then the localized application to the joints will usually give the desired relief. In some cases where it is impossible to find any remnant of the local infection, but where joint, muscle, and nerve pains persist, it is frequently possible to elevate the temperature of the blood by general methods of application. In these cases, we find the multiple electrode method and heavy currents effective. Kraft and Ten Doesschate have reported successful results in three cases of gonorrhoeal conjunctivitis. They find that the heat generated within the tissues by diathermy reaches a higher degree than is possible to attain with compresses, cataplasms, etc.

Bumm found that the gonococci lost their power of reproduction at 100° F. if the heat was long continued. A degree of 110 can be reached by diathermy in the conjunctiva. The eyes of rabbits withstand a degree of 114, without apparent harm. A mercury thermometer placed in the cul-de-sac, the scale projecting from between the lids, can be used to measure the heat. Ordinarily, the patient's sensation may be our guide. The heat generated in the eyeball is retained mostly in the tissues which offer the greatest resistance to the current, the cornea and the sclerotic.

The success of a first case was most striking. Two years later a second presented. Two hours after the application of diathermy for fifteen minutes, no further gonococci could be found in the secretions of one eye. Those in the other eye disappeared by the

tenth day. The third case had an ulcer of the cornea and the skin of the eyelids was macerated by preceding local applications of permanganate of potassium and silver salt solutions. On account of the great sensitiveness of the eyes in this case, diathermy could not be applied in the most effective manner, yet, in spite of this, the gonococci finally vanished. Briefly speaking, we have frequently obtained very good results by currents of relatively low amperage, with attention given to the greatest possible concentration of heat effect.

The pneumococcus also succumbs to the diathermic heat. Acute pulmonary congestion can usually be promptly arrested if diathermy is early applied to the walls of the chest by suitable metal plate electrodes. The course of bronchitis may be shortened. Frequently it may be aborted. As Dr. H. E. Stewart has given the results of his studies of diathermy in pneumonia, we will only say here that some of our earliest work with high-frequency currents was in the treatment of pulmonary disorders. In August, 1905, a case of pneumonia did not clear up by the usual methods of treatment. However, the fever and pulmonary infiltrations, which persisted, yielded to five applications of the direct d'Arsonval current applied with metal plates. In 1906, a similar case, where the process had lasted two months, yielded also to five applications.

We need not assume that the heat effect is alone the cause of the beneficial action in cases of bacterial invasion. The rousing to normal activity of the circulatory apparatus as the result of the active arterial hyperæmia, the increased flow of lymph, the opening of the natural channels to the phagocytes, the freeing by heat of the circulation from poisonous gases, all contribute their share to building up the natural defences of the body.

In cases of chronic ethmoiditis, good results were obtained by applying diathermy by means of metal plates. One of these is placed over the forehead and the other to the occiput just below the hair line. Sometimes this may be supplemented by a cross-fire effect, applying a metal plate to each temporal region. Moderate current strength should be employed, 250 to 400 milliamperes by means of electrodes of equal size; $1\frac{1}{2}$ to 2 inches square being the rule. Diathermy should only be applied if good drainage is present. Violation of this rule will result in intensifying the pain and other manifestations. It may even lead to feverishness and extensive mus-

cular soreness. Used carefully as stated it has resulted in improving the eyesight where the impairment was due to the ethmoiditis.

Diathermy applied to the head is one of our best weapons in senile changes in the brain, causing marked impairment of the mental faculties, though they do not always lead to apoplexy.

It is also useful in many cases of nervous breakdown, as the result of overwork or the gradual accumulation of toxic materials in the general circulation. These toxic materials may be of intestinal origin, may result from chronic fatigue, or be introduced from without. Alcoholic abuse, the introducing of poisonous minerals into the system or the absorption of poisonous gases, belong to the latter category.

Applied to the head as described, the diathermic current must pass through the pituitary body and through the centres of the vegetative nervous system, which govern all of the excretory functions and the activities of the endocrine system. Thus we readily understand the widespread beneficial effect, as observed, on bodily functions. The very existence of life is dependent on the activities of the vegetative system. The heat centres, the respiratory centre, the centre of metabolism and that of water regulation have been proven, experimentally, to reside in the third ventricle.

Diathermy, properly applied to the head in moderate dosage, has a general tonic and reconstructive effect on the entire system; in addition to its purely local effect.

In conclusion, because of its action on the sympathetic and the autonomous nervous system, we may expect certain definite clinical effects in disorders of the circulatory apparatus. Also in other states of disordered function resulting from pathological changes of different degrees.

TREATMENT OF LOCAL INFECTION *

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It is the purpose here to consider the types of infection associated mainly with pyogenic processes, rather than the types of infection that are found with serious constitutional symptoms from the outset. The latter have been more successfully controlled or prevented by antitoxins or prevented or ameliorated by immunization. The successful control and limitation of smallpox by the institution of vaccination by Jenner before the revelations of Pasteur was a forerunner of what has made possible the now scientific prevention or amelioration of typhoid fever, spinal meningitis, diphtheria, tetanus, scarlet fever, and other serious diseases. The same measures, however, have been *far less* successful in controlling and preventing the pyogenic infections of various types. It is with these that electrical and other thermic measures and forms of radiant energy play an important rôle which will be now considered.

The sources of pyogenic infection are either from within or without the host. The alimentary tract is a suitable culture media for the development of bacteria within the host, particularly the colon bacilli—the Gram negative—and the streptococci or staphylococci—the Gram positive. From that source it varies with the habits and relative resistance of the host, for, as has been tritely stated by Zinsser,¹ “The actual harm resulting from the infection must, to a large extent, depend upon the degree of adaptation to the new condition of life possible on the part of both the invader and the host.” With these premises the indications are to fortify the host against the invader. With a normal healthy organism and the alimentary canal functioning in a regular manner and the diet regulated to the body’s requirements, the alimentary flora cannot become a menace which will favor the absorption and extension of pyogenic infection

* Read before the joint session of the American Electrotherapeutic Association and allied societies at the Academy of Medicine on Wednesday, January 6, 1926.

¹ “Immunity and Infection,” Zinsser, p. 7.

elsewhere. In the normal individual, the active phagocytic processes, both leukocytic and lymphoid, are ample guard against furunculosis or the production of abscesses emanating from within. With this conceded, the indications, when the conditions have not given adequate protection, and, for obvious reasons, to prevent the invasion, are to raise or increase the resistance of the tissues invaded, destroying the local infection. It is apparent then that to accomplish the overthrow of the invaders the tissues must be fortified by bringing a larger army of phagocytes into the field, and, if possible, otherwise impair the resistance of the invader.

During the past quarter of a century attention has been frequently called to the importance of fortifying an infected area by increasing the flux of arterial blood into the infected tissues. The induction of local hyperæmia, as stated in an Editorial²: "The employment of heat in various ways—sinapisms, dry and wet cupping, blisters, and massage, all of which induce various degrees of local hyperæmia—is as old as the practice of medicine. In the affections to which hyperæmia is adapted, its use is invaluable, but the methods of its induction for local effects are manifoldly greater, and by far more valuable than some recent advocates of the Bier school have considered it. Cupping, cording, and the employment of dry hot air are the methods which they especially advocate. Far better in selected cases is the employment of high-frequency currents or the use of radiant light and heat energy by both local and general methods of application." The attention of the Association was again called by the writer to the subject in March, 1910,³ as follows: "The application of radiant light and heat and convective heat and high-frequency currents, each in its particular way, while inducing hyperæmia, coincidently inhibits the vitality and activity of germs in a local region of infection. The effect of prolonged exposure to intense light is recognized as adverse to the activity of all forms of life. The actinic properties are even destructive to some forms of germ life, while extreme degrees of heat also inhibit and render temporarily

² "The Relation of Induced Hyperæmia to Therapeutics," *Am. Journ. Electrotherap. and Radiol.*, March, 1907, p. 145.

³ "The Rôle of Physical Therapeutics in the Treatment of Infection," *Am. Journ. Electrotherap. and Radiol.*, March, 1910, p. 111.

inert all germ life, and the coincident induction of hyperæmia increases the circulatory activities."

*The value of hyperæmia*⁴ as a therapeutic agent requires no argument, for it is self-evident that where hyperæmia is present, as induced by a natural physiological stimulus, there is (1) increased nutrition relative to the increased quantity of blood passing through the tissues; (2) the activity of the cellular elements is also stimulated, with a consequent increase in local metabolism; and (3) a greater number of phagocytes is carried in and out through the tissues. Elimination, phagocytosis and the tissue-producing processes of the body are thus accelerated. The administrations become a matter of degree which must depend upon the length of the radiation and the temperature tolerated by the patient. It has been found, from the practical point of view, that toleration, that is within the range of comfort, not extreme, is the best rule for intensity of dosage, and that the average period of application should be at least for one hour.

The practical means of effecting hyperæmia which are available and valuable are reflected radiant light and heat from an electric arc or incandescent bulb or bulbs, dry hot air applied with suitable electric or gas-heated apparatus, and diathermy from a high-frequency electric transformer. These facilities are now available in most well-appointed hospitals and sanitariums. The technic of employing each is as follows:

Reflected radiant light and heat is applied from large or small therapeutic lamps depending on the area to be exposed. Candle-power signifies nothing more, as penetration is the same for like qualities of radiant energy and skin toleration is the limit of dosage. The carbon-filament incandescent lamps are richer in penetrating infra-red or so-called "heat rays." The small therapeutic lamps made for this purpose employ 100- to 200-watt bulbs with a stereoptican carbon filament.

TECHNIC

*Position.*⁵—The position of the patient should, as a rule, be reclining and comfortable, and the source of the rays should be so

⁴ "Use of Radiant Light and Heat in the Treatment of War Wounds," Snow, *Am. Journ. Surg.*, Sept., 1917.

⁵ "Thermotherapy," Snow. The George Blumer Edition of Billings-Forchheimer's "Therapeusis of Internal Diseases," Vol. I, 1924, p. 348.

placed that the radiations will be projected perpendicularly upon the surface requiring treatment.

Distance.—The distance from the reflecting source of light should be adjusted to the comfort of the patient with a degree of heat always verging on discomfort—very warm.

Extent of Exposure.—The extent of exposure, as previously stated, should be decidedly larger than the area of involvement, but should be so limited as not to cause discomfort from relatively heating unnecessarily parts not requiring it. This may usually be regulated by the use of a small light apparatus for a small area and larger lamps or applicators over the body and extensive surface regions.

Length of Exposure.—The time required should be, in nearly all conditions, when not otherwise specified, at least one hour for each administration. In cases of severe conditions, as of erysipelas or abscesses, the one-hour exposures should be frequently repeated or continuous, and continued until severe symptoms have subsided.

The use of dry hot air in the treatment of local septic infection, as far as the literature reveals, was first published by Dr. Clarence E. Skinner,⁶ who, in the course of a general treatment given in a case of infection, discovered the marked fall in temperature and improvement of the local infection received from the treatments. The principle upon which the treatments devolve is the proper wrapping of the arm or limb in Turkish toweling and then subjecting it to the heat applied in a proper dry hot-air apparatus, either heated by gas or electricity, which is capable of giving a temperature of from 300 to 500° F. The heat applied in this manner has a very important effect on the process. The development of germs seems to be arrested, if they are not destroyed, from the first, and the active process subsides from the first application. This, however, must be applied with the proper technic to accomplish any result. Treatments should be for from one-half hour to one hour daily, and all collected pus in the cellular tissue should be first evacuated.

Surgeons and students of the Bier school of hyperæmia have not seemed to appreciate the real effect of dry heat as applied by the method described. The following quotation from Kanaval clearly indicates that the effect on the initial lesion is not considered impor-

⁶ *Journ. Advanced Therap.*, Feb., 1903, p. 92.

tant from the point of view of destroying the bacteria in the part affected. Kanaval⁷ quotes Auchincloss as having made "extensive use of dry hot air," and quotes him as having had "most satisfactory results in so treating infected hands." Kanaval further states that it gives comfort and adds to recovery after hot fomentations, with the statement that "the idea seems perfectly rational," and concludes with the statement that he uses this procedure in nearly all cases.

This indicates the limited concept of the real potency of a measure which, if used during the first few days instead of after a few days, with the proper energy, would promptly terminate the infection. When concluding his consideration of the management of lymphangitis, Kanaval prescribes "hot, moist dressings applied voluminously until the infection is walled off."

When the surgeons cease to use hot, moist dressings which, at best, give only the effects of convective heat, from which hyperæmia occurs only in the skin, and the heat is carried away with the circulation without affecting the cellular tissues beneath the skin, and when they adopt the use of dry heat from the outset, they will have most satisfactory results, but not so long as they continue to employ wet dressings as described by Kanaval.

Frequent deaths of surgeons and physicians from lymphangitis each year indicate the failure of the profession at large to recognize the importance of the measures that will control or terminate lymphangitis.

The following case well illustrates this state of mind: Dr. M., an operating surgeon from Toronto, Canada, received a slight infection on the posterior aspect of his right hand after an operation. This was followed by an extensive lymphangitis confined mostly to the hand, which finally resulted in producing a complete incapacity of the right hand for operative procedures. He came to me with the statement that his "surgical career was ended," wishing to familiarize himself with physical methods of treatment which he could carry out as I have with crippled hands. He had been in the best clinics in America, and had been advised to leave it to nature and he concluded "that was what he had done, and here it is, a useless hand." Upon examination it was discovered that, although there were two sinuses discharging between the sheaths of the tendons on the posterior aspect, no tendons were adherent within the sheaths. There was also necrosis at the end of the digit of that hand. I told him that from my own experience I saw no reason why his hand should not be entirely restored except for a shortening of the digit. He was quite astonished, after having consulted

⁷ "Infections of the Hand," Kanaval, p. 79, 1925.

eminent surgeons, that I should make such a statement. I gave him four local treatments with hot air and had him use a therapeutic lamp over the hand for one hour twice each day at his room. The sinuses promptly closed and the hand made a progressive improvement with the uses of heat and the application of manipulation and mechanical vibration over the stiffened muscles. In three weeks a hand which had been crippled for three months was completely restored to usefulness.

I mention this case merely to show that the eminent surgeons of the country are not conversant with this procedure. This is not said as a reflection on them, but as a statement of the fact and to urge them to become familiar with a method which is practical and efficient. It is for consideration of this class of cases and for others that will follow that this subject was chosen for this occasion. During the past twenty-five years we have used methods of employing heat in infection in a large number of cases and without failure in arresting the process in all early cases.

For one surgeon I have employed this method on three occasions and he is one of the most grateful friends I have, and one of the most earnest advocates of the method. If the infection is noted by the surgeon on the first day or within twelve hours following the signs of infection by the presence of a persistent red spot on the hand, one two-hour application of radiant light projected over that spot, as hot as can be tolerated, will terminate the trouble.

The late Doctor Ochsner related a personal experience to me when I called on him at his office in Chicago in the summer of 1917. He had been suffering from a severe lymphangitis and "the pain was agonizing." One of the physicians suggested: "Why don't you try light on it?" Doctor Ochsner said, "What will that do? Use anything!" The light was administered and the relief from pain was almost instantaneous and his arm was soon well. When a surgeon receives an experience of this sort, he becomes an advocate of the measure, as did our lamented friend, Doctor Ochsner.

The following observations, made by the writer with Doctors Grad and Munday,⁸ suggest another serious infection in which dry heat would seem to be indicated. "A patient in extremis with general septicæmia, three weeks after a difficult surgical operation, with the

⁸ "The Therapeutics of Radiant Light and Heat and Convective Heat," Snow, 1909, p. 97.

characteristic feeble pulse, livid countenance, and a temperature of 105° F., was wrapped by the usual method in Turkish toweling and placed in a body hot-air apparatus and the temperature raised to from 300° to 350° F. After thirty minutes, she was removed with a strong pulse, a marked hyperæmia of the skin, and a mouth temperature of 103° F. Eight hours later the temperature was normal, and in ten days the patient was convalescent. This extraordinary result could only be explained by (1) the induction of an active phagocytosis with a positive chemotaxis; (2) stimulating by heat of the deep spinal centres, particularly the cardiac and respiratory; and (3) the elimination of toxins and other bodies through the agency of the profuse elimination produced by the high temperature."

Diathermy is another important method of applying dry heat, and is especially indicated in internal infections as in *cholecystitis*, *subacute and chronic appendicitis*, *sinusitis*, *pneumonia*, *bronchitis*, *pleurisy*, etc. The administration is made with the same rules of application as with other heat administration, limited to skin toleration. The electrodes applied should be considerably larger than the area affected and placed with the centre over the part, and an indifferent electrode of the same size over an opposite area. The current should then be gradually raised to skin toleration, and the treatment continued for at least thirty minutes or, in many cases, for a full hour.

Infections about the Head.—There is probably no region where a pus process is more dangerous in cases where there may be an extension of a septic process than in infections about the face and head. Numerous deaths are reported of people who have died from operations in these cases. It is far more judicious and generally successful to permit the infection either to go on its own way until it discharges or to terminate it by some physical measure. The following case will illustrate the management of such a condition:

Dr. L., a practising physician, developed a very severe and painful abscess just above the angle of the jaw. It had developed to a diameter across the base of fully an inch and a half and the attending physician was loath to operate, owing to the fact that similar cases had terminated fatally when operated upon. I advised and arranged to have a small therapeutic lamp delivered at his house, to be applied constantly, with the result that the whole condition resolved without any further treatment. This might be an unusual result but it indicates that a very serious process was developing which the application of reflected radiant

light and heat promptly arrested before a pus cavity had formed. My advice in this instance would have been to persist in the use of light until an evacuation had taken place rather than to have an operation in any way. By this means, the walls of the pus cavity discharging outward would not permit the extension of the septic process, whereas if an incision were made a channel might be opened through which the infection could extend.

Other cases about the head, which may be considered here, are *mastoiditis* and *otitis media*. The method of managing these cases by the use of reflected incandescent light was first published by Dr. Herbert E. Pitcher,⁹ of Haverhill, Mass., in which he gave an account of the successful treatment of cases both of *otitis media* and *mastoiditis* with reflected incandescent light. Since the publication of this report, we have used this method in a very large number of cases, few of *mastoiditis* because, as a rule, these cases should be treated with circumspection and only employed with patients who refuse operation. With the *otitis media* cases, which, as a rule, lead up to *mastoiditis*, it is quite a different matter. These purulent cases are promptly relieved by the use of reflected incandescent light. The administration should be made for at least one hour daily and persisted in until the discharge ceases. In acute cases the relief of the pain in *otitis media* is remarkable, and unless the case is to be operated on by a specialist, it is far better to allow the membrane to rupture than to allow any operation, for, if light is applied twice daily for an hour each time after the first escape of pus, the ear will recover its normal condition in from seven to ten days, which is a more favorable result than usually follows a paracentesis.

*Purulent and gonorrhœal ophthalmia*¹⁰ are two classes of cases which will afford considerable satisfaction to the physician who applies reflected incandescent light over the eye with the lid closed for one hour twice daily in any suspected or established case. Numerous cases have been reported with successful results in these conditions.

⁹ "Phototherapy in General Practice," Herbert F. Pitcher, M.D., *Journ. Advanced Therap.*, Sept., 1906, p. 433.

¹⁰ M. M. Thompson, "A Case of Ophthalmia Neonatorum Cured by Radiant Light," *Am. Journ. Electrotherap. and Radiol.*, July, 1919, p. 209.

Louis L. Gannett, "A Case of Ophthalmia Neonatorum," *Am. Journ. Electrotherap. and Radiol.*, May, 1922.

F. S. Holliday, "Gonorrhœal Ophthalmia in an Adult," *Am. Journ. Electrotherap. and Radiol.*, April, 1921, p. 159.

The following case¹¹ was the first reported as treated by radiant light and heat:

"In the winter of 1919, Dr. M. M. Thompson, Captain, M.C., of Piteairn, Pa., in charge at the Port of Embarkation at Hoboken, when handling gonorrhœal cases became infected in one eye and the surgeons diagnosed the condition as gonorrhœal ophthalmia. On hearing of his predicament I at once ordered a fifty candle-power therapeutic incandescent lamp sent to the hospital. The surgeons had put him to bed, and he was suffering excruciating pain from the infection. When the lamp arrived he applied it as hot as he could stand the radiations, and reported that after half an hour's application the pain had ceased. He adjusted the lamp on a stand at a distance from the bed at which he could tolerate the heat and lay with the light shining upon his eye for the whole night. In the morning when the surgeon came to his room he found the patient's eye was open and free from pain, though deeply injected. The surgeon asked what he had been doing. He pointed to the lamp, and the surgeon remarked, 'We are never too old to learn.' He continued the use of the light for three days, after which time the eye was normal. I believe that this was the first case of gonorrhœal ophthalmia treated in this manner."

In erysipelas,¹² in which the writer has had an opportunity of employing radiant light and heat, results have proved very satisfactory. These cases were treated at the onset, and the applications were made for from one to four hours, no administration being made for less than one hour in the manner described. The result in each case was complete arrest of the erysipelatous condition. In one case the œdema of the face had closed both eyes. After four hours' exposure to intense radiation—two hours in the morning and two in the afternoon—the œdema disappeared. Two additional exposures on the two following days restored the features to normal.

The following case reported by Doctor Bingham,¹³ of New York, will illustrate the measure of success obtained even in a very bad case, treated by an eminent surgeon.

"A patient with facial erysipelas had received no treatment for several days after its inception, and the disease was well advanced. One eye was entirely closed by the swelling, and the other nearly so. All the features of the face were practically obliterated, and one ear was very badly swollen and painful.

"I had light applied for an hour's duration, five or six times the first day,

¹¹ "The Treatment of Local Infection by Physical Measures," Snow, *N. Y. Med. Journ. and Rec.*, Mar. 21, 1923.

¹² Sajou's "Analytic Cyclopedia of Practical Medicine," seventh edition, Vol. 6, 1914, p. 361.

¹³ James R. Bingham, "A Case of Erysipelas Treated by Reflected Radiant Light," *Am. Journ. Electrotherap. and Radiol.*, Dec., 1918, p. 320.

and twice during the first night, as the patient was wakeful. During the second day the light was applied less often, and for shorter periods, and as the patient slept all during the second night it was not applied at all.

"From the beginning the pain was markedly relieved by each treatment, and after the first day, there was absolutely no pain complained of by the patient.

"The swelling and redness began to recede from the first application of the light, and at the end of forty-eight hours the only manifestation of the disease remaining was a slight swelling of the involved ear, which entirely disappeared on the third day after a few short applications of the light."

Many cases of erysipelas treated in this manner have been reported and in no instance has there been a failure to affect complete relief by the use of radiant light and heat in the treatment of these cases. There are already on record a considerable number of cases to warrant the belief that this will become the established method of managing this troublesome condition.

The X-ray plays no small rôle in the treatment of local infections whether singly or in association with other methods. It is uncertain just what the effect upon the bacteria is, but they are destroyed. The writer assumes that it is accomplished by the process of sterilization and inhibition as upon other forms of life that their development is arrested, so terminating their kind. Be this as it may, it has been established that the X-ray does play an important part in the treatment of *tuberculous adenitis* and *other tuberculous affections* and in the treatment of *infected tonsils*.

Diathermy is particularly indicated in the treatment of *internal infections* in which it is generally used in conjunction with the X-ray. The treatment of *bronchitis* and *pleurisy* with diathermy and the X-ray gives most satisfactory results.

In *pneumonia* there is no longer any question as to the part diathermy plays in the treatment. In conjunction with radiant light and heat in this condition, the fact that the cases terminate with lysis beginning with the first administrations is positive proof that the treatment by heat is at least affecting the arrestment and promoting the termination of the process.

Diathermy and the X-ray in *cholecystitis* and *subacute and chronic appendicitis* have established their value beyond question.

The treatment of sinusitis has been generally successful by the use of reflected incandescent light, but the more recent adoption of the use of diathermy has demonstrated its superiority in these cases.

However, when the high-frequency current is not at hand the use of reflected incandescent light is eminently successful in treating this condition, likewise in the treatment of acute coryza when a few one-hour applications will terminate the affection.

It will be seen from the above that the employment of heat in its different forms, ultra-violet rays and the X-rays, fills a very important rôle in the management of a class of cases which has been generally more or less neglected or left to nature, as it is said "nature and the knife," are either arrested or cured as by no other means.

CONCLUSIONS

(1) The relation of the host to the invader from within or without is such that the first indication for treatment of local infection is to fortify the part invaded and destroy the invader.

(2) The induction of active local hyperæmia by modalities that heat the tissues and so, in response to normal reflexes, increase the circulation in the parts involved, coincidently depresses or destroys the germs present.

(3) Under conditions of active hyperæmia, nature's scavengers, the phagocytes, clear out the invading bacteria.

(4) The modalities instrumental in the accomplishment include reflected radiant light and heat, dry hot air, diathermy with the direct d'arsonvâization, X-rays and ultra-violet rays.

(5) Properly administered, these measures constitute most important means for coping with all types of local infection.

RADIOTHERAPY OF THE BLOOD AND LYMPH-TISSUES

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To THE ordinary individual there would seem to be little, if any, relation between blood affections, such as leukæmia and pernicious anæmia, and neoplastic growths of the nature of sarcoma or carcinoma. Among pathologists, however, the conviction is steadily growing that certain blood diseases, as well as some pathologic processes such as those productive of lymphosarcoma and Hodgkin's disease, are in reality tumors of the hematopoietic or lymph systems, and should, therefore, be amenable to the same therapeutic measures which have been found useful in frankly neoplastic growths such as sarcoma and carcinoma. The considerable measure of success which has attended the application of radium to many diseases of the blood and lymphatic systems bears out these observations.

The reason for the beneficial effects which radium irradiation has upon those types of blood diseases allied to neoplastic processes thus becomes very obvious, but when we reach the consideration of the anæmias we find ourselves on more uncertain ground. Though many observers have reported that favorable results have followed the application of irradiation in pernicious anæmia, the balance of evidence seems against, rather than for, it. Extensive studies at the Collis P. Huntington Memorial Hospital upon the effects which irradiation has upon the blood, have brought to light some facts which may have a bearing upon the somewhat vexed question of the exact effect of irradiation under conditions not at present very well understood. It has been found that "the most important effect of customary therapeutic doses of irradiation on the blood elements is to decrease the number of white cells, especially lymphocytes, so that leukopenia and lymphopenia may occur. Preceding the decrease in the white count a transient increase develops, due to increment of polymorphonuclear neutrophils. Very small doses of irradiation may permit a lymphocytosis."

It was found by Millet and Mueller that the immediate effects

of radium on the blood consisted of a drop in the total white count which reached its maximum from one-half to six hours after the radium application, and returned to its original level within twelve hours or possibly twenty-four hours, with an occasional secondary rise to a point well above its original level, this secondary rise usually taking place in from twelve hours to three days after the radium application. There is a close adherence of the total polymorphonuclear count to the total white count, but no characteristic changes in the total lymphocyte and large mononuclear counts. There is also a tendency of the total lymphocyte count to drop, and of the polymorphonuclears to rise during the course of treatment. This tendency was noted to be reversed immediately following the withdrawal of the radium.

Remote effects—noted two to four weeks after irradiation—were a fall in the lymphocyte count which sometimes lasted until another month had passed, and a diminution in the number of polymorphonuclears, sometimes synchronous with the lymphocyte fall, but often coming later and being less marked. Later on the lymphocytes make an effort to recuperate, as from three to nineteen weeks after treatment they have been noted to increase until their number approximated that existing before radium application was made.

A consideration of these points does not lead us to expect beneficial results from irradiation in such blood diseases as pernicious anæmia. It would seem that radium treatment would be useful in hyperplasia rather than hypoplasia of the blood elements. Gulland, professor of clinical medicine in the University of Edinburgh, remarks that no one would attempt to treat secondary anæmia by radiating the spleen or the long bones, though “chlorosis—if it is really due to an excess of blood-plasma and the attempt of an overworked marrow to keep the plasma full of corpuscles—might conceivably be treated by radiation.” To be sure “pernicious anæmia does present a hypoplasia in the elements which promote the formation of both red and white corpuscles.” Gulland believes that the hyperplasia of the bone-marrow noted in pernicious anæmia “is due to the fact that the death-rate of the red corpuscles is high, and regeneration requires to be as rapid as possible. Obviously, therefore, it must not be checked, and radiation is contra-indicated.”

Other investigators, however, are not in accord with his views. For example, Ferdinand Tománek, a Slavic internist, considers pernicious anæmia as a primary idiopathic hyperplasia of the spleen with increased hemolytic activity which inhibits the erythropoietic function of the bone-marrow. He does not believe that any treatment can do more than shorten the florid stage and increase the time length of the remissions. Removal of the spleen may stimulate erythropoiesis, but it has only a temporary effect, and in his experience radium applications are quite as effectual as the operative removal of this organ.

In general, it may be said that though pernicious anæmia has been subjected to radium in a considerable number of instances, the patients so treated are still too few in number and the results too various, and too much influenced by other factors, to permit of generalization which would have any value either for or against the use of radium. It can be said, however, that in all cases where radium applications have been made over the spleen, that organ has shrunk to its normal size, a result which could be attributed to nothing else but the irradiation.

Lymphatic Leukæmia.—There is a marked variation in opinion as to the benefit which a subject of lymphatic leukæmia may hope to derive from radiotherapy. Gulland found radium unsuited to this form of leukæmia, though he used it successfully in the myeloid type. The experience of Aikins, the Canadian radiologist, and several others in this country was similar, but Levin, on the contrary, produced "excellent immediate clinical results" even though the final outcome was not satisfactory, which he thinks "probably due to the fact that leukæmia is a systemic generalized disease from its incipience."

It was found by Minot and Isaacs that lymphatic leukæmia is undoubtedly benefited symptomatically by properly administered radium therapy, though the effects were, on the whole, not as satisfactory as in the chronic myelogenous form. "The beneficial effects of irradiation in acute lymphatic leukæmia" they found "but evanescent and slight." If the patient's hemoglobin was 50 per cent. or less, there was little hope of improvement under radium treatment, and, in any event, the decreasing effect of succeeding radium expos-

ures in reducing the size of the spleen or the lymph-nodes "is apt to be proportional to the amount of improvement in the patient's general sense of well-being." The treatment must be carefully checked up with the physical signs and the history in each case, and frequent complete blood examinations and determinations of basal metabolism are very essential. As the disease progresses the radium treatment will become less and less effectual, but it nevertheless not only considerably prolongs life, but enables the patient to go about his daily affairs in comparative comfort, so that existence is made much more bearable than is the case with those who do not get the benefit of irradiation.

Chronic Myelogenous Leukæmia.—In this rapidly fatal disease, radium therapy has proved a decided boon, even though figures—such as those compiled by Minot and his co-workers—indicate quite definitely that irradiation does little, if anything, toward prolonging life, for there is no doubt that the treatment is of sufficient value to these unfortunate patients, to provide strong indications for its use whenever possible. No form of therapy hitherto tried has given the same amount of symptomatic benefit, and permitted the patient to maintain his efficiency so that he could continue his ordinary mode of life for so long a time. "Continued irradiation, properly administered, offers the best guarantee of the longest possible preservation of the patient's working capacity. An adequate dose of radium or röntgen-ray causes, as a rule, striking general clinical improvement coincident with the approach to normal of the formed blood elements and basal metabolism." More than half of these patients so improve that from being in many cases completely bedridden, they return to a state of comparative well-being, so that to the layman, many seem entirely well.

The changes undergone by the blood of the myelogenous leukæmia patient have been intensively studied. Röntgen-rays and radiation with radium or its emanation have an apparently identical action upon the blood in this disease, provided that the radiation is of the same quality. Some workers believe, however, that radium is somewhat quicker and more reliable. The fact that limited doses of radium produce a stimulating effect upon all hematopoietic centres is, in the opinion of Strumia, borne out by the increase in the number

of leukocytes and erythrocytes, and by the increase in the number of immature—that is, nucleated—red cells, especially of the megoblastic type which are in evidence after only a few radium applications have been given. The knowledge of this stimulating action is of great importance as it suggests the possibility of treating primary anæmia by small applications of radium, though the precise manner in which radio-activity acts upon the blood of the leukæmic patient is not yet clearly understood. It may very well be brought about by a combination of the destructive action upon the red cells with diminution in the formation of granular leukocytes, and of an accompanying exaggerated production of red cells. Levin believes that the myelocytes of myeloid leukæmia, which can so readily be destroyed by radiation, represent biologically a different type of cell, probably more akin to a cancer-cell. It is a remarkable fact that local irradiation of the spleen alters the blood-picture, although the myelocytes are derived mainly from the bone-marrow.

It has been experimentally demonstrated that the larger the square surface of the entry of radium or X-ray into the organism, the more severe is the general effect upon the blood. As this destructive action is exactly what we wish to obtain in leukæmia, it becomes desirable to bring about as extensive radiation as possible, so that instead of tubes of radium we prefer to make use of large flat applicators properly screened, which are laid over the splenic area. These are usually left in place for a length of time sufficient to produce a slight erythema. As much as 2500 to 3000 millicurie hours may be given at a single treatment by shifting the applicator according to a system of squares plotted out beforehand on the skin surface over the spleen, these squares corresponding to the size of the applicator.

Apparently the quality of the radiation is of more importance than the particular body area to which it is applied, for in any event the entire body will receive more or less effect from the irradiation. The successful results obtained from radiating the spleen alone are probably due, in the opinion of Strumia and others, to the extreme vascularity of this particular organic structure. A large part of the circulating blood must pass through it, and is thus brought in direct contact with the action of the radium.

Lymphosarcoma is a malignant disease of the lymphoid tissue which is evidenced by a rapid proliferation of the cells of the lymph-

nodes, so that they invade the adjacent tissues by breaking through the capsule of the gland. It is most often encountered in the glands of the mediastinum, or of the gastro-intestinal tract. The type of cells which increase may be either the lymphocyte cells or those of the reticulum, but proliferation of the lymphocytes is decidedly more common. A careful study of this condition has revealed that "lymphosarcoma is only a manifestation of a systemic disease which embraces the whole lymphoid system." It is, therefore, of no avail to resort to surgical removal of the sarcomatous tumors in any part of the lymph system as "a discrete tumor of lymphosarcoma is always surrounded by diseased lymphoid tissue, and the operation is followed not only by recurrence, but by the development of the latter tissue into new tumors."

Radiotherapy, therefore, offers practically the only hope of alleviation. Skinner, of Kansas City, has reported a number of cases where patients had remained without recurrence for more than six years after the tumors had subsided following radiation, with either röntgen-rays or radium. The radium dosage is 100 milligrams, at a distance of one inch, that is, 2.5 cm., usually applied in tubes of radium emanation, or needles screened with lead and brass. The entire tumor area is plotted out, and applications made over the surface until a total radiation of from twelve to eighteen hours has been given.

Hodgkin's disease has been very satisfactorily treated by radium, though our experience has led us to believe that we must all agree with Stone when he says "it is of practical importance to accept its incurability as a fact in order to obtain the best palliative results." In a series of 164 cases he succeeded in bringing about marked palliation in 60 per cent. and there is a possibility that in as high a percentage as 32 "complete restoration of health, with or without complete regression of the tumors" may be temporarily brought about; this intermission lasting for at least a year, and in some cases for as long as five years.

Many observers testify to the great usefulness of radium in this distressing condition. Aikins found there were no characteristic changes in the blood following the irradiations, but that improvement was evidenced by the reduction in the size of the enlarged glands and increase in the patient's bodily strength and general sense of well-

being. Burnam observed that chronic cases of Hodgkin's disease are more amenable to radium treatment than those of more acute type. "In a chronic case limited to one set of glands, a single exposure may lead to a cure, which has, in one case, lasted over five years." Heavy exposures in acute Hodgkin's disease are usually followed by rapid reduction in the size of the gland masses, but with no corresponding improvement in the blood or the patient's general condition. In these acute cases, rest in bed, forced feeding and mild fractional radiation are indicated. The chronic cases which do not display marked glandular enlargement, though the patient exhibits decided constitutional evidence of disease and a greatly altered blood-picture, are the most unpromising from the viewpoint of the radiologist. If the infection is circumscribed, appearing only in isolated gland groups, as in the axillary and cervical regions, radium applications will almost always render the glands no longer palpable, but in widely extended involvement, especially if seated in the mediastinum, the outlook is much more unfavorable. In the chronic form of Hodgkin's disease the immediate effects are excellent; the enlargement of the gland subsides, the blood-findings improve and the patient's general health is markedly benefited.

Radium emanation is usually employed for treatment, a fifty-milligram tube, most commonly made of silver, 0.5 mm. in thickness, with a lead filter 2 mm. thick. This is held at a distance of perhaps 2.6 cm. for a period of time varying from three to eight hours. In certain cases it may be best to keep the tube in place for an entire twenty-four hours. If the enlarged glands are numerous and scattered, the radium applications must be correspondingly distributed, and in all cases great care should be exercised to prevent producing an erythema.

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CONTRA-INDICATIONS TO THE USE OF RADIUM IN GYNÆCOLOGY

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THE standardization of the indications for the employment of radium, its proper dosage, and the development of the proper technic of its application have engaged the attention of serious clinical and laboratory workers for the last fifteen years. Those of us who have labored conscientiously to fix those standards and who appreciate the splendid therapeutic qualities of radium, as well as its inherent possibilities for damage, cannot but view with misgivings its indiscriminate use by inexperienced physicians who know little or nothing of the physical properties of the agent they are employing, and probably as little of the pathology of the processes for which it is being applied.

Dr. W. J. Mayo, in one of his happy colloquial moments, once said that many physicians were "buying a nickel's worth of radium and doing a million dollars' worth of harm with it." This witticism expressed a truthful situation when uttered, and the seriousness of it is more obvious now when large quantities of radium are available in more communities and are more accessible to any physician who wishes to employ it.

The brilliant possibilities of radium in surgery and gynæcology have no doubt led to much of its misuse and the rapidly widening field of its employment. The indications for its use are now fairly definitely defined; the dangers of misapplication and over-dosage are equally well known. It has not proved to be the panacea it was first thought to be, nor are its uses so general as it was first hoped they would be. It has been definitely shown that its results are unsurpassed by those of any other therapeutic agent in certain conditions, when wisdom and judgment are used in the proper selection of cases for treatment and the irradiation is employed by one possessing the necessary experience in its application.

It is being employed too frequently by the general practitioner and the röntgenologist, both of whom lack the discriminating knowledge of the various pelvic diseases as clinical entities, as well as of the

more satisfactory results which may be obtained by other methods. For example, it is generally known that radium is the remedy *par excellence* for uterine hemorrhage, but what pathology underlies the bleeding, and whether irradiation is the method of choice in a particular instance is another matter, one which is too often disregarded.

Before proceeding to discuss the contra-indications for the use of radium in diseases of the female genital tract, it is well briefly to mention the three great indications for its use, cancer of the cervix, uterine myoma, and metropathic bleeding. No other therapeutic agent is more effective or has a more general field of application than radium in cancer of the cervix uteri. It may be safely stated that there are few cases which cannot be benefited to some extent by its employment. Some authorities, it is true, still advocate operation in the early cases, and unfortunately there is still some confusion in the minds of some physicians as to just what type of case should be classified as early, but, on the whole, a study of large series of comparative cases treated by these two methods will show the results in favor of radium. Granting that there may be sufficient reason for resorting to surgery in the extremely early case, there is no longer any question as to the wisdom of irradiation in the border-line and advanced case. These patients become clinically well, live comfortably, often for years, and even though they finally succumb to the disease, they are spared the suffering from chronic infection and sloughing processes because the end usually results from metastasis and is fairly rapid.

Again, radium has proved its worth beyond question in the treatment of certain selected cases of uterine fibroids. It is an ideal agent in women over thirty-eight or forty years of age, in whom the preservation of function is not of great importance, the growth not larger than a 3 or 3½ months' pregnant uterus and of the interstitial type, and the appendages are free from pathology. These conditions are met with in approximately 30 per cent. of the fibroids causing symptoms in white women, and therefore nearly one-third may be satisfactorily relieved by irradiation.

Lastly, in the treatment of the metropathies, insufficient ovarian function and the chronic hyperplasias so frequently associated with the menopause, radium stands out practically as a specific.

The contra-indications to the use of radium in gynæcology are quite as important as the indications we have just outlined. Even in

cancer of the cervix, for instance, we must emphasize the fact that in at least one group of these cases irradiation will bring disaster. I have reference particularly to cases so far advanced that there is extension to the rectum and bladder. In these, if radium be applied in sufficient quantities to affect the malignant process, the danger of sloughing and fistulæ is so great that any possible benefit from the application is more than overbalanced by the added suffering from its effects. Cases so far advanced as this are frankly hopeless, and irradiation will very likely increase their already unhappy state. It should also be very cautiously employed in the type of case in which the pelvic cavity is choked with malignant masses which practically fix all the pelvic structures. Severe bleeding is frequently associated with this condition, and although it may be controlled, the ultimate result is very far from satisfactory.

Radium is definitely contra-indicated in cancer of the body of the uterus, both because surgery is so eminently satisfactory in this condition, and also because experience has proved that the results are by no means so good as they are in cancer of the cervix. Surgery has to its credit a high percentage of permanent cures, and, moreover, because of the known tendency of malignancy of the fundus to metastasize to the ovaries, oöphorectomy is usually indicated also, which makes opening the abdomen a necessary factor in the cure of the average case. Again, cancer of the body is usually of the adenocarcinomatous type, which experience has proved does not readily respond to irradiation. In my early work, before our indications had been standardized, I treated several cases of this sort with radium. Most of them did badly, the majority of them complained bitterly of the persistent and profuse foul discharge which ensued, and at least three of them developed a definite pyometra.

The field of irradiation is limited, as I have already pointed out, in the treatment of uterine fibroids by certain strict indications, which will obviously leave some two-thirds of these cases to be handled by other methods. Irradiation in the uncomplicated case under thirty-eight should be considered distinctly more radical than surgery because of the grave danger of producing a permanent amenorrhœa. To secure the desired results, the radium must be used in sufficient quantity to check menstruation for a period of months, and since, in our present state of knowledge, we cannot control its action in these

larger doses, we are obviously gambling with a dangerous stake when we use irradiation as the elective treatment for fibroids in young women. In this connection I would make a plea for a procedure long in disfavor but in recent years gradually coming into its own, the operation of myomectomy. It is unquestionably the more conservative procedure in any case in which it can be performed because of the chance it offers for the preservation of the functions of menstruation and child-bearing, with a mortality and morbidity no higher than that of the average major abdominal operation.

Irradiation does not influence to any perceptible degree pedunculated, subserous or submucous growths, and it is especially undesirable if uterine polypi are also present. I stress this fact particularly because I am seeing patients almost weekly who have had radium applied without a diagnostic curettage, which to my mind is indicated before every intra-uterine application, or without a careful investigation as to the type of growth present. Such tumors, on the other hand, are frequently influenced badly. The trauma incident to the diagnostic curettage and the manipulation necessary in the application of the radium element, as well as the resulting reaction of the structures, too frequently result in the sloughing and infection of the growth to warrant its use under such conditions. In a few such instances I have applied radium against my better judgment, where the growths were large or of the submucous type, because the symptoms were urgent enough to need control and there were contra-indications to operation, and more than once I have regretted my decision. In one case the patient developed a large pelvic abscess which confined her to bed for weeks, and when I last heard from her I could not see that the symptoms from the tumor had been relieved any. I might add that in the treatment of fibroids with a moderate amount of radium, the application should be in the cavity of the uterus.

Radium is absolutely contra-indicated in the presence of chronic pelvic infections, particularly salpingitis, whether of specific or puerperal origin. Such cases call for the closest discrimination in diagnosis, and furnish one of the chief reasons why, as I have already said, an experienced clinician should direct the use of this remedy. A carefully interpreted history is necessary, with an extensive pelvic examination, for often these lesions present no gross manifestations, and if these precautions are ignored, it is surprising how frequently

severe inflammations supervene and terminate in pus collections in the pelvis, which require radical surgery for their removal. This is one of the obvious reasons why radium must be carefully limited in the treatment of fibroids. A fair percentage of the larger growths are associated also with adnexal disease, especially chronic salpingitis, and this is particularly true among colored women, where such growths, because of their great size and the frequently accompanying adnexal pathology, almost invariably demand surgery for their cure.

To my mind radium is usually contra-indicated in the treatment of ovarian pathology. It leads to misfortune when used in the presence of cystic ovaries, peri-oöphoritis, and degenerative changes associated with fibroids. In more than one of my early cases it seemed to me that cystic changes in the ovary were actually aggravated and the size of the ovary increased by irradiation. The epochal work of Sampson on endometrial transplants and our realization that these may involve not only adjacent structures but also remote ones should make use doubly careful in eliminating chocolate cysts of the ovary and similar pathology before we decide upon irradiation. I can think of few conditions in which this treatment could cause more disastrous results than in the presence of endometrial implants into the ovary, when rupture has taken place and adhesions have formed.

Because of its known effect on the ovarian function, which is believed by many to be the principal factor in its success in controlling uterine hemorrhage, radium has been advocated in certain instances to bring about sterilization. Its use in this field is open to very serious question. When sterilization is demanded within the child-bearing period for legitimate and ethical reasons, surgery is certainly preferable. The latter is also my preference in the occasional case which demands the cessation of menstruation for the relief of intractable dysmenorrhœa. We cannot ignore the problem which this type of case presents, but to my mind we can best meet it by hysterectomy, in spite of the slight added risk, because of the violent menopausal symptoms which radium may produce in a young woman. At best the menopause, artificially produced, is an individual problem in every instance, and any procedure which leaves a functioning ovary is certainly to be preferred to one which does not.

Radium is occasionally advocated in the treatment of chronic endocervicitis, and Curtis, of Chicago, has reported almost uni-

formly good results by this method. He is a careful diagnostician and a skilled pathologist, and his results are therefore beyond question, but I should hesitate to commend the procedure to the profession at large. Such a condition is frequently associated with low-grade tubal disease, and irradiation may be the means of fanning into activity a latent virulent infection. In view of the safety of other methods, the electrocautery, the Stürmdorf operation, or merely trachelorrhaphy, I can see no reason for employing a procedure which obviously carries with it a definite element of risk.

Radium has also been advocated in some quarters for the treatment of urethral caruncles and chronic urethritis of the lower half inch of the urethra, usually associated with chronic infection of Skene's glands. I have personally used it for this condition in about six cases, and my final conclusion is that each of them could have been handled better by the proper surgical procedure. I have also seen cases from other clinics treated by this method, and the results have been uniformly poor. In some instances the caruncle has disappeared, but the pain has been persistent, or even aggravated. In two instances which I have observed recently a marked contraction of the urethra has required slow and tedious dilatation, and in two other instances the peri-urethral infiltration was so marked that I have been treating the patients for more than two years without as yet giving them full relief.

I have not, as you might infer from these warnings, become skeptical in regard to the value of irradiation. On the contrary, the longer I use it the more enthusiastic I am in regard to its actual results and its possibilities. But, as the years have passed, I have become increasingly cautious in its employment and increasingly fearful of its potentialities for harm. Unless it is used in selected cases, chosen according to strictly defined indications, and unless it is employed by men who are skilled diagnosticians and clinicians, with a wide knowledge of pathology, anatomy and surgical technic, disaster is certain to follow and a valuable remedy will be discredited in the eyes of both the profession and the laity. Legal regulation of its use will never, I think, be either wise or practical but certainly it behooves those of us who were the pioneers in its use and who have increasing faith in its benefits to sound a note of warning in these days when it is being employed promiscuously on flimsy indications or on none at all.

Medicine

PARAPLEGIA IN LYMPHOGRANULOMATOSIS MALIGNA (HODGKIN'S DISEASE) AND LEUKÆMIA, AND THE QUESTION OF THERE BEING A "HODGKIN SARCOMA" AS WELL AS A "HODGKIN GRANULOMA"

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(1) IN A paper in 1923 on "Paraplegia and Cauda Equina Symptoms in Lymphogranulomatosis Maligna (Hodgkin's Disease)," ¹ I described the case of a young man who in 1918, at the age of eighteen years, had had some enlarged glands excised on the right side of his neck. Microscopical examination then and later showed the disease to be typical Hodgkin's disease. Under treatment of various kinds the general condition of the patient remained fairly good till February, 1921, when he complained of severe lumbar pain. By May, 1921, more or less actual paraplegia had developed, and early in July the plantar reflexes on both sides were noted to be of the extensor kind (Babinski's sign). In May, also, considerable pyrexia of "hectic" type commenced, which continued in greater or less degree till a few days before the patient's death on December 6, 1921.

The *necropsy* showed masses of enlarged retroperitoneal glands and other enlarged abdominal lymphatic glands—typical of lymphogranulomatosis maligna. There was no evidence of tuberculosis in the lungs or elsewhere. The moderately enlarged spleen (weight, 17 ounces) contained yellowish nodules. There was considerable fibrosis of the lymphatic glands about the vertebral column; but quite distinct from that was a remarkable thickening of the periosteum on both outer sides of the vertebral centra about the region of the diaphragm. Microscopical examination of this periosteal growth proved it to be of true lymphogranulomatous nature, containing endothelial-like cells and lymphogranulomatous giant cells. On opening the vertebral canal lymphogranulomatous growth of the

¹ F. PARKES WEBER, *Quart. Journ. Med.*, Oxford, 1923, Vol. xvii, pp. 1-5.

same character was found attached to the outer side of the dura mater over the end of the spinal cord and farther down over the cauda equina; the lymphogranulomatous process had, in fact, involved the loose connective and fatty tissue between the spinal dura mater and the vertebral bone; the only question was whether this post-mortem finding was sufficient to account for the paraplegic symptoms observed during life.

(2) In a clinically somewhat similar case described by Eichhorst,² the patient, a boy aged seventeen years, who was supposed to be suffering from myeloid leukæmia, developed signs of spinal cord involvement two or three weeks before his death. The post-mortem examination showed a growth in the spinal canal at the level of the fifth to seventh dorsal vertebræ, loosely connected with the bone and the spinal dura mater and compressing the spinal cord. Eichhorst himself was not convinced that the case was one of leukæmia, and from his description of the microscopical appearance it seems probable that the growth in the spinal canal was lymphogranulomatous in nature, involving the peridural (epidural) fatty tissue.

(3) In the case of a man, aged forty-six years, described by W. B. Warrington in 1911,³ there was a history of primary syphilis nine years previously, but microscopical examination pointed to a mass of lymphatic glands (of about three years' duration) on the right side of the neck, being of the nature of Hodgkin's disease (lymphogranulomatosis maligna). The patient later on developed paraplegia and died. At the necropsy white nodules in the spleen and liver confirmed the diagnosis. The paraplegia was due to a mass of growth that had eroded the bodies of the eighth to twelfth dorsal vertebræ and had grown downwards along the dura mater compressing the spinal cord.

(4) In J. E. Welch's case of a woman, aged thirty-two years,⁴ to which I shall refer further on, paraplegia arose in the course of lymphogranulomatosis maligna and was shown by post-mortem examination to have been caused by a metastatic tumor-mass of the spinal dura mater. There was amyloidosis of the spleen.

(5) In C. W. Suckling's case (1885) of Hodgkin's disease (diag-

² H. EICHHORST, *Deut. Arch. f. klin. Med.*, Leipzig, 1898, Vol. lxi, p. 519.

³ W. B. WARRINGTON, *Liverpool Med. Chirurg. Journ.*, 1911, Vol. xxxi, p. 52.

⁴ J. E. WELCH, *Proc. N. Y. Path. Soc.*, 1910, new series, Vol. x, p. 161.

nosis made at the time), with symptoms of pressure on the spinal cord, there were multiple growths from the dura mater.⁵

(6) L. R. Shore and W. A. Young⁶ have recently (1925) described the case of a woman, aged twenty-six years, with abdominal lymphogranulomatosis maligna and amyloidosis; the bodies of the eleventh dorsal and second lumbar vertebræ were infiltrated. The patient had complained of pain in the right lower extremity.

(7) S. Rosenstein⁷ published the case of a boy, aged seven years, with "pseudoleukæmia," who became paralyzed in the legs. At the necropsy the dorsolumbar region of the spinal cord was found diseased, but nothing abnormal was noted outside the dura mater, either in the vertebral canal or in the vertebræ.

(8) In the case of a woman, aged forty-four years, with Hodgkin's disease, described by G. A. Allan and J. W. S. Blacklock,⁸ death was connected with paraplegia, bed-sores, and septic meningitis. At the necropsy the paraplegia appeared not to have been connected in any way with the lymphogranulomatosis. Degeneration of the crossed pyramidal tracts was demonstrated from cervical to lumbar region; above the mid-dorsal region it was incomplete; below that level it was complete; there was myelitis below the mid-dorsal region.

(9) A very interesting case was that of a Jewish man, I. H., aged fifty-one years, to which Dr. S. Sacks drew my attention. He was said to have had diphtheria and diphtheritic paralysis of the larynx and soft palate. He also had incomplete paraplegia and loss of knee-jerks. Unfortunately no blood-count was made during life, and he died (1924) on the second morning after admission to the London Hospital. Dr. H. M. Turnbull, Director of the Pathological Institute of the London Hospital, very kindly wrote me the results of the careful post-mortem examination. The case was one of true myeloid leukæmia with tumor-like (sarcomatoid) infiltrations in various parts. The cause of the paraplegic symptoms was well explained by the necropsy findings. The extrathecal adipose tissue of the vertebral canal, especially round the exit of the spinal nerves,

⁵ C. W. SUCKLING, *Lancet*, London, 1885, Vol. i, p. 246.

⁶ SHORE and YOUNG, *Lancet*, London, 1925, Vol. ii, p. 915.

⁷ S. ROSENSTEIN, *Arch. f. path. Anat. u. Physiol.*, Berlin, 1881, Vol. lxxxiv, p. 315.

⁸ ALLAN and BLACKLOCK, *Glasgow Med. Journ.*, 1925, Vol. ciii, p. 115.

was infiltrated, the infiltration forming a hard mass round the cauda equina. There was likewise infiltration within the dura mater below the exit of the third lumbar roots, affecting the posterior roots of the fourth lumbar segment and all the spinal nerve-roots below this level.

(10) Doctor Turnbull tells me likewise of a boy, aged fourteen years, with Hodgkin's disease and general amyloidosis, who died in 1911. The patient's spastic paraplegic symptoms were found at the necropsy to be connected with syringomyelia. There was cavitation of the third to the ninth segments of the dorsal spinal cord. But Doctor Turnbull could find no histological evidence of any direct connection between the lymphogranulomatous disease and the syringomyelia.

(11) Doctor Turnbull has kindly told me of yet another case in which Hodgkin's lymphogranulomatosis was associated with nervous symptoms. The patient was a man, aged twenty-nine years (1911), and the symptoms in question were due to a cellular pachymeningitis interna complicating the lymphogranulomatosis. The slight thickening of the inner, areolar, layer of the dura mater was granulomatous, but had not the characteristic cytology of Hodgkin's lymphogranuloma.

(12) In regard to the occurrence of paraplegia in leukæmic cases I would refer to a specimen of chloroma in the vertebral canal of a boy, aged fourteen years, shown by Drs. A. C. Sturrock and Jeffery, of Manchester, at a pathological meeting of the Neurological Section of the Royal Society of Medicine, May 14, 1925. Paraplegia had developed suddenly four weeks before the patient's death.

(13) I am indebted to Dr. J. A. Ryle, of Guy's Hospital, London, for notes on a case (1924) of clinically typical Hodgkin's disease, observed during three years in the Out-patient Department. With the help of röntgen-ray therapy the enlarged glands in his neck, which were the first ones to become apparent, almost completely disappeared. Then the patient developed a large, painful lump under the liver. With deep röntgen-ray therapy this melted away and all local symptoms disappeared. He then quite suddenly lost all power in his lower limbs and developed rectal and bladder incontinence. The spinal cord lesion was localized to above the fourth

dorsal level. He was given some deep radiations here, but without benefit, and died. The necropsy confirmed the diagnosis of Hodgkin's disease. There were some lymphogranulomatous plaques on the front of the bodies of the vertebræ, but none of these appeared to track upwards through the spinal foramina. One very minute deposit only was found in the theca, and there was nothing exerting pressure on the spinal cord. At the level suspected there was simple softening of the cord over an area of two or three inches, so that the paraplegia in this instance complicating the Hodgkin's disease was not due to compression. There was no history of syphilis and the Wassermann reaction was negative.

(14) To Dr. H. L. Tidy I am greatly indebted for a report on a man, W. W., aged forty years (in St. Thomas's Hospital, London), who suffered from Hodgkin's disease, and developed paraplegia some time before he died (January, 1924). The necropsy confirmed the diagnosis of Hodgkin's disease. In regard to the vertebral column and spinal cord I will quote the following: A large mass of growth was present on the anterior aspect of the vertebral column from the sixth to the tenth dorsal vertebræ. It appeared in the form of two long, thick cords giving an appearance as though enlarged glands had fused together. Growth was also present on the lateral aspect of the spine in this locality and also in relation to the necks and adjoining portions of the ribs. Another patch of growth was in relation to the tenth and eleventh ribs, the central end being contiguous with that on the vertebral column. From the level of the first lumbar vertebra two long cylindrical masses of growth, again suggesting the appearance of enlarged and fused glands, extended along the anterior aspect of the spine to just beyond the bifurcation of the abdominal aorta. The aorta was surrounded by this growth and was freed by dissection. No direct invasion of the aorta was present. The inferior vena cava lay on the right side of the growth and was only slightly involved by its presence. Growths were present in the spinal canal on the posterior aspect of the cord extending from the sixth to the tenth dorsal vertebræ. Four processes were present on each side of this mass and were due to the fact that the growth had made its way into the canal through the spinal foramina. With increase in size fusion between the various

portions of growth from the different points of entry had evidently taken place. Small nodules of growth were present in the erector spinæ in the lower dorsal region. The necropsy notes from which I have been kindly allowed to quote are by Dr. J. Bamforth. The microscopical examination of portions of various enlarged lymphatic glands and growths showed lymphogranulomatous structure (Hodgkin's disease).

(15) Sir William Osler had a case of Hodgkin's disease, in which paraplegia was due to lymphogranulomatous growth within the vertebral canal, but I have not been able to find the account of the case.

(16) K. von Müllern and B. Grossmann⁹ have described the case of a man, aged twenty-eight years, in whom lymphogranulomatosis maligna was associated with tuberculosis. Some of the vertebræ were infiltrated with tuberculous material and with tissue resembling lymphogranulomatosis maligna in structure. This vertebral disease, which involved the dura mater and actually compressed the spinal cord, was at least in part of tuberculous nature.

(17) In the discussion on my paper in 1923 (above referred to) Sir W. Hale-White mentioned a case of Hodgkin's disease with upper limb involvement, due to compression of the roots of the brachial plexus by growth within the vertebral canal. Though not a case of paraplegia it should also be referred to here.

(18) M. Askanazy (*Verhandl. d. Deut. path. Gesellsch.*, Jena, 1921, xviii, p. 78) described a case of lymphogranulomatosis maligna with involvement of the spinal column (a true "spondylitis lymphogranulomatosa"). The periosteum and spinal dura mater were infiltrated at the level of the fifth cervical vertebra.

(19) Schmorl (*ibid.*, p. 82) mentioned an analogous case of "spondylitis lymphogranulomatosa."

(20) Dietrich (*ibid.*, p. 83) referred to a similar case that he knew of.

DISCUSSION

In the preceding notes I have referred only to cases in which a post-mortem examination was made; other cases have come to my

⁹ VON MÜLLERN and GROSSMANN, *Ziegler's Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1912, Vol. lii, p. 276.

notice,¹⁰ but the above-described examples suffice to show that in lymphogranulomatosis maligna and leukæmia complicated with more or less paraplegia, the post-mortem findings in regard to the cause of the spinal symptoms differ in different cases. In by no means all the cases was there tumor-like growth affecting the vertebral column or within the vertebral canal. In one case (No. 10) there was an association with syringomyelia, which gave rise to the cord symptoms. In another case (No. 11) there was a curious kind of cellular pachymeningitis interna, the exact nature of which was not obvious. In one case (No. 16) the tuberculosis associated with the lymphogranulomatosis maligna was probably responsible. In other cases (Nos. 7, 8, 13), however, a myelitic or parenchymatous change in the spinal cord itself seems to have been the cause of the paraplegia.

A question which one may ask is: Can deep röntgen-ray treatment (with the newer forms of apparatus) ever give rise to transverse degenerative changes in the spinal cord, leading to paraplegic symptoms? The question may well be asked, since it is now recognized that deep (intensive) X-ray treatment of mammary carcinoma or affected axillary glands may, in rare cases, give rise to pulmonary fibrosis.

THE QUESTION OF A "HODGKIN SARCOMA"

A consideration of the tumor-like (neoplastic-like) masses of growth present in some of the above-described cases of lymphogranulomatosis maligna brings us now to another question. Does the disease in any cases assume a true neoplastic sarcoma-like character, clinically and macroscopically—in other words: Does a "Hodgkin sarcoma" arise out of a "Hodgkin granuloma"? James Ewing¹¹ holds that it does, and so, apparently, does K. Ziegler, and so also do Hudelo, Cailliau, Mouzon and Oury.¹² I suppose that a "Hodgkin sarcoma" of this nature is the same as Pappenheim's "granulo-

¹⁰ Dr. H. L. Tidy tells me of a man, aged about forty-two years, in whom cauda equina symptoms first attracted attention to the presence of any disease. This patient has now a mass of enlarged lymphatic glands on one side of the neck, which "biopsy" microscopical examination shows to be lymphogranulomatous.

¹¹ EWING, "Neoplastic Diseases," second edition, 1922, p. 373.

¹² *Presse méd.*, Paris, 1923, xxxi, p. 729 (report).

sarcoma." Douglas Symmers¹³ divides his cases of Hodgkin's disease into two groups: (1) The ordinary well-known kind of case; and (2) cases in which the disease causes infiltration and destruction of muscles, blood-vessels, serous and mucous membranes, erosion of bone and mechanical replacement of solid viscera. According to Ewing,¹⁴ mediastinal Hodgkin's disease furnishes a large proportion of the cases terminating in sarcoma.

The structure of Hodgkin sarcoma, he says, varies from a close counterpart of Hodgkin granuloma to a tissue composed exclusively of large, round cells. Large, round, giant cells with multiple or multi-lobed nuclei may predominate. The proportion of lymphocytes may be considerable, as in Karsner's case (that he quotes), but in the more definite neoplastic processes these cells are missing. The structure may not be uniform in all the lesions nor at all periods. Many cases described in the literature of the subject as lymphosarcoma are, according to Ewing, probably examples of Hodgkin's sarcoma. The histological signs of malignancy, he says, may not be very pronounced and it is difficult to decide when the lesions first become malignant. The exact position of this form of sarcoma is, he says, difficult to determine; its clinical malignancy may depend on the dissemination of an infectious agent or its toxins, and the local recurrences are probably recrudescences in new lymphoid structures. Yet, he adds, the metastatic growths in the dura mater and lung and the changes in the type of the cells demonstrate the malignant tumor nature of the growth (compare his reference to J. E. Welch's case in particular).

These considerations would account for some of the cases in which paraplegia or symptoms of compression of the cauda equina supervene in patients suffering from typical Hodgkin's lymphogranulomatosis. I have shortly described such cases in the first part of this paper, and amongst them is J. E. Welch's¹⁵ case which Ewing¹⁶ cites as a typical example. The latter case was one of Hodgkin lymphogranulomatosis in which an enlarged cervical lymphatic gland, removed six months before the patient's death, showed a lymphogran-

¹³ SYMMERS, "The Clinical Significance of the Pathological Changes in Hodgkin's Disease," *Am. Journ. Med. Sci.*, Philadelphia, 1924, Vol. clxvii, pp. 313-339.

¹⁴ EWING, *loc. cit.*

¹⁵ WELCH, *loc. cit.*

¹⁶ EWING, *loc. cit.*

ulomatous structure. The post-mortem examination showed that the paraplegia which had arisen was due to a metastatic tumor-like mass of the spinal dura mater, and "tumors" removed at the necropsy from the neck, dura mater, liver and lung "showed replacement of lymphocytes, chiefly by large, round cells resembling sarcoma."

In cases of so-called "mediastinal Hodgkin's disease" there may be a very large tumor-like mass in the mediastinum which causes death without giving rise to metastatic tumors and on microscopical examination the mass may present a typical lymphogranulomatous structure. This was so in the case described by Dr. J. C. G. Ledingham and myself in 1907,¹⁷ but in a recent case, under the care of my colleague, Dr. H. Rast, the mediastinal tumor infiltrated the sternum, some of the ribs and the lungs. By the kindness of Doctor Rast, who showed me the patient, I am now enabled to give a short account of the case, in which a careful post-mortem examination was made by our pathologist, Dr. E. Bock.

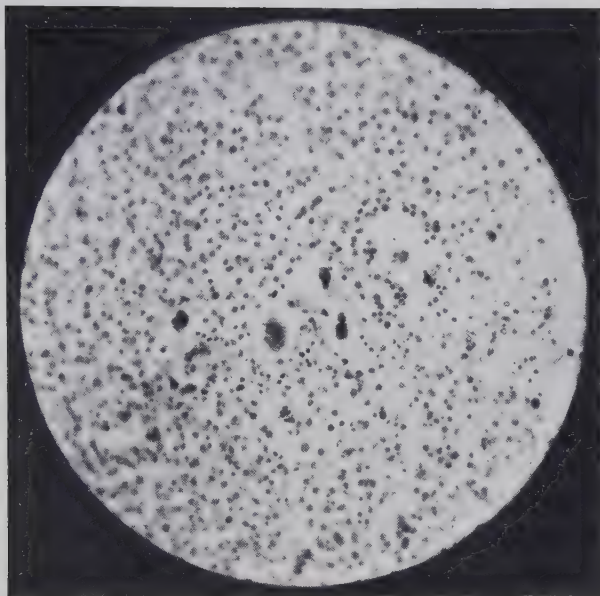
The patient was a married Swiss woman, aged thirty-eight years, living in London. In October, 1923, she consulted Doctor Rast about a swelling at the sternal end of the third rib on the right side. Doctor Rast was not satisfied that this was of tuberculous nature and did not favor the idea of her going abroad for treatment in a sanatorium for tuberculosis, although there was a history of previous tuberculous peritonitis about the year 1908. An excised piece of the tumor was examined microscopically and was regarded as sarcomatous by one pathologist and as perhaps syphilitic by another. Syphilis, however, could be practically excluded; the Wassermann reaction was repeatedly negative.

In April, 1925, the mediastinum was found to be extensively involved and the lymphatic glands in the right axilla and on the left side of the neck were infiltrated; there was also pyrexia. A lymphatic gland removed from the right axilla (April, 1925) showed (Doctor Bock) a typical lymphogranulomatous change with endothelial-like cells and "Hodgkin giant cells." This diagnosis, which was supported by Dr. Herbert Fox, of Philadelphia, an authority on lymphatic glandular diseases (then on a visit to London), explained a temporary improvement which at one time had taken place under neosalvarsan injections. In May, 1925, a blood-count gave 4,000,000 red cells and 6300 white cells per cubic millimetre of blood; of the white cells 78.5 per cent. were polymorphonuclear neutrophils, 9.0 per cent. were lymphocytes, 10.0 were monocytes, and 2.5 per cent. were eosinophiles.

Later on, in spite of treatment by sodium cacodylate, the patient became steadily worse. She looked weak and anæmic, complained of general cutaneous

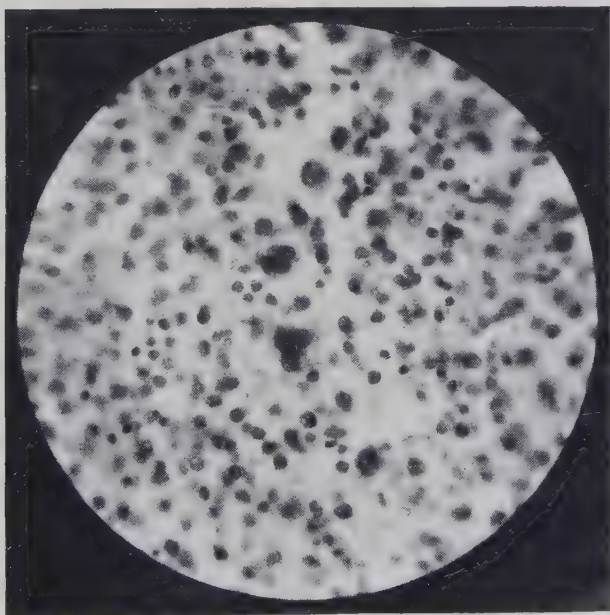
¹⁷ F. PARKES WEBER and J. C. G. LEDINGHAM, "Mediastinal Form of Lymphadenoma (Hodgkin's Disease)," *Proc. Roy. Soc. Med.*, Clinical Section, London, 1909, Vol. ii, pp. 66-86. There were no metastatic growths beyond infiltration of some of the cervical lymphatic glands.

FIG. 1.



Microscopic appearance of the great mediastinal tumor, magnified 240 times.

FIG. 2.



Tumor under still higher magnification (500 times).

pruritus (a characteristic symptom in some cases of Hodgkin lymphogranulomatosis) and had an up-and-down pyrexia, with a morning temperature of about 36.6° C. and an afternoon temperature of about 38.8° C. She died on August 22, 1925, from suffocation owing to the intrathoracic tumor.

For the results of the necropsy, including the microscopical examination, and for the microphotographs, I am indebted to our pathologist, Dr. E. Bock. There was a hard, white mediastinal tumor which infiltrated the sternum, some of the ribs, the greater part of both lungs, and involved the parietal and visceral layers of the pericardium. There were no metastatic growths in other viscera, excepting some minute (microscopical) foci in the liver. The spleen showed amyloidosis, but no lymphogranulomatous changes. Otherwise, nothing of consequence was found, excepting that both fallopian tubes were adherent to the posterior wall of the uterus (in this connection one should remember the history of peritonitis about 1908).

Fig. 1 shows the microscopical appearance of the great mediastinal tumor, magnified 240 times. Fig. 2 shows the tumor under still higher magnification (500 times). The resemblance of the structure, notably the giant cells, to that of Hodgkin lymphogranulomatosis is obvious.

MASSIVE COLLAPSE OF THE LUNGS

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1. Introduction.
2. Definition.
3. History.
4. Incidence of massive collapse as a complication of the diseases of the chest.
5. Incidence of massive collapse as a post-operative complication.
6. Incidence of massive collapse as a complication of wounds of the chest.
7. Incidence of massive collapse as an association with foreign-body inhalation.
8. Anatomical findings and conditions.
9. Etiology.
10. The clinical picture of massive collapse.
11. The physical signs of acute massive collapse of the lung.
12. Differential diagnosis from other intrathoracic conditions.
13. The diagnosis of massive collapse after operation from other known post-operative cardio-respiratory accidents.
14. The diagnosis of a massive collapse from other thoracic complications occurring after a wound of the chest or lung.
15. The prognosis of massive collapse of the lung.
16. Treatment of massive collapse of the lung.
17. Plates, references, cases of massive collapse.

A GLANCE at the medical literature of to-day on the subject of massive collapse of the lung shows plainly that the ideas of William Pasteur¹ have been fully substantiated and that his prophesies are in a fair way to being completely fulfilled. As far back as 1908, this writer declared that there was a lung condition, occurring acutely after operation, usually called pneumonia, but associated with such physical signs that an acute massive collapse of the lung rather than consolidation was suggested. In pursuing his investigations Pasteur noted that Pearson Irvine² had described a massive collapse of the lung following diphtheria, and occurring apparently in association with paralysis of the diaphragm, he was moreover well aware of the fact that the blocking of the trachea or bronchi might cause a complete and rapid collapse of the lungs even without an accompanying pneumothorax, but he nevertheless very properly claimed that he was describing a condition whose relationship to operation had not as yet been suggested, a condition, the significance of whose physical signs must have escaped the observation of generations of clinicians.

Massive collapse of the lungs following an operation is now a condition recognized in all clinics as a curious accident most often met with after the inhalation of foreign bodies into the air passages and subsequent to abdominal operations; the similarity of its physical signs to those of consolidation of the lungs has allowed it to go unchallenged until detained for our observation by Pasteur's discerning hand. The degree of the contraction of the affected side, the extent of the mediastinal displacement described as part of the accident, and the acuteness of the onset in many cases, tells us loudly that only too often must this, the most interesting of the invaders of the post-operative period, have come before unseeing eyes; even to-day the recognition of the meaning of unilateral consolidation with displacement of the mediastinum to the affected side seems to have spread further amongst our surgical colleagues than amongst us the clinicians. That this is so is due largely to the excellent descriptions appearing from the surgical experiences of Elwyn,³ Lee,⁴ Barling,⁵ Crymble,⁶ Scrimger,⁷ Leopold,⁸ Hirschbroek,⁹ Scott,¹⁰ Chevalier Jackson * and others; the accounts of the earlier and more purely medical writers, Pasteur, Elliott and Dingley,¹¹ and Rose Bradford,¹² have never attracted amongst clinicians the interested attention they deserve.

Definition of Massive Collapse of the Lung.—Massive collapse of the lung is a more or less acutely occurring complete atelectasis of a lobe, a lung or lungs; most often recorded in the past after operations upon the abdomen, and looked upon as a complication of surgery, it nevertheless has a medical bearing in that it may complicate pericardial effusions, pulmonary inflammations, pleural affections and paralytic states of the diaphragm; its association as a quickly fatal process terminating conditions of obstruction in the upper air passages has been reported by laryngological surgeons¹³; it was a not uncommon happening in the course of the wounds of the chest as seen in the late war.

* The numerous papers from the bronchoscopic clinic of Chevalier Jackson have indicated very positively not only that massive collapse has an existence but that it is a very frequent complication of the inhalation of foreign bodies into the air passages. To the excellence of his descriptions nothing can be added and in this paper we have preferred to treat foreign-body collapse as the special property of the bronchoscopists and to leave it for their description, merely touching on the question of its incidence.

History.—Massive collapse of the lower lobes and one instance of complete atelectasis of an upper lobe was described by Pearson Irvine in 1872. Diphtheritic paralysis of the diaphragm and of the accessory muscles of respiration seemed to explain the condition in these cases by interfering with the proper aëration of the bases and apex, respectively; complete and rapidly developing atelectasis of both lungs subsequent to persistent laryngeal and tracheal obstruction or to acutely occurring occlusions of the air passages is detailed from the clinics of St. Clair Thompson and C. L. Starr.† Lichtheim¹⁴ demonstrated that a massive collapse could be induced in the animal lung by obstructing a bronchus with a plug; as a clinical entity, however, and as a finding with any but pathological interest, the condition seems to have completely escaped the many observers who had investigated post-operative pulmonary complications or who may have recorded the course of acute and chronic inflammations of the lungs and pleuræ.

Beginning in 1908, William Pasteur, of the Middlesex Hospital, issued a series of articles in which he showed that after abdominal operations, particularly if a general anæsthetic had been used, there might be seen occasionally a condition of the lungs much resembling a consolidation, but differing from it in that marked displacement of the mediastinum into the consolidated area could be demonstrated. The state of affairs in the chest, according to his demonstrations, was, further, not in accordance with effusions and their results, and he described the happening as an acute lobar collapse. Elliott and Dingley confirmed Pasteur's observations, as did Tidy,¹⁵ in the year 1914, and the great war showed conclusively that even a very obvious condition may at times remain undetected in the face of the keenest investigation, for at this time massive collapse came to be recognized as a common complication of chest wounds, yet it is not to be doubted that the campaigns of the centuries must have produced many thousands of examples of this, the most interesting of chest conditions. The contributions from the surgical clinics in recent years allow one to conclude that the accident of massive collapse has acquired recognition from the surgeons. It still appears, however, that many of the more purely clinical workers are unfamiliar with the descriptions of Pasteur, Rose Bradford and the other English writers which put so

† Wookey, referred to by Gwyn, *Tr. Asso. Amer. Phys.*, 1923.

clearly before us the fact that a very distinct clinical entity had long lain concealed in the obscure pile of acute respiratory distresses.

Incidence of Massive Collapse as a Complication of Diseases of the Chest.—Only in very recent years has the existence of an acutely occurring massive collapse of the lungs been considered. In no author's contributions can one see an estimate as to the frequency with which massive collapse may complicate the course of a pneumonia, a pericardial effusion or a pleurisy; the accident of an acute atelectasis must have been often overlooked and lost in the diagnosis of heart failures, embolism, progressive lung involvement or acute pulmonary oedemas. One realizes that the sudden urgencies in our cases of pleural effusions which were not attended by rapid increases in the amount of the fluid and which we so often attempted to relieve by aspiration, may be explained by the suggestion that a hitherto unaffected part of the lung had become suddenly atelectatic. A massive collapse possibly accompanies some of the embolic and infarctive lung accidents, the partial collapse of the left lung or its base, in association with pericardial effusion, is a closely allied process, though it lacks, as a rule (but by no means always), the dramatic element of the acute lobar form. Rose Bradford's description of collapse of the lung bases, in association with the paralysis of the diaphragm in the polyneuritic cases of the later years of the war, details yet another form of more or less acutely occurring atelectasis.¹⁶ It has long been recognized that asthenic individuals, who have lain long on their backs, may show a condition of collapse, more or less complete, of the undermost parts of the lungs. Pathologists of to-day are describing with much greater frequency areas of massive collapse in the lungs of patients dying from other affections of the thoracic organs.

Incidence of Massive Collapse as a Post-operative Pulmonary Complication.—Pasteur says that massive collapse ranks third in order of frequency in the lists of post-operative pulmonary complications; lobular pneumonia and embolism are the only accidents found in greater numbers as primary lesions. If the clinician will look with suspicion on all post-operative pulmonary lesions which are limited to one side, it is probable that the incidence of massive collapse as a surgical complication will be found to be considerably higher than the present conservative estimates indicate. Less than 2 per cent. of the cases in the analysis of the instances of post-

operative pulmonary complications from the clinic of Prof. C. L. Starr suggested massive collapse, but it is to be noted that mediastinal displacement was rarely looked for as an essential part of the examination; the numerous instances of unilateral consolidations recorded after operations, in the face of the fact that post-operative pneumonias are lobular in type and should be bilateral in distribution, suggests that a reconsideration of physical signs and diagnoses would show a material increase in the number of cases labelled "massive collapse of the lung." A critical examination of the diagnoses marked post-operative pulmonary embolism and infarction will show the same omission as regards the determination of the cardiac and mediastinal areas; massive collapse is probably more often hidden by the pre-formed idea of embolism than by any obscuring cloud of physical signs. It can be very properly urged that unilateral pulmonary affections following surgical operations be systematically investigated with the idea of the detection of a massive collapse in view.

More commonly seen as a complication of abdominal operations, massive collapse must nevertheless be considered as an associated possibility wherever in operations elsewhere in the body, thrombosis of large veins with subsequent pulmonary embolism may threaten the lung, or where in operations on bones or fatty tissue, there may occur the less commonly met with cases of fat embolism; any pulmonary irritation—inhalation, embolism, infarction—added to the hampering conditions of the operation as concerns the movement of the diaphragm—may set going the mechanism by which the acute atelectasis is induced.

Incidence of Massive Collapse as a Complication of Wounds of the Chest.—During the war of 1914–1918 the importance of Pasteur's observations became apparent; it was early announced by Rose Bradford, by Sir George Meakins, by T. R. Elliott and by Pasteur himself that massive collapse was a frequent concomitant of chest wounds, and that either the undamaged part of the wounded lung might collapse suddenly and give rise to fresh distress or that even the sound lung might react to the wound in the other side of the chest and by its rapid collapse produce symptoms which would be ascribed to the existing wound. In two thousand cases of wounds of the chest the writer saw twelve outspoken examples of acute massive collapse of one or the other lung, an incidence of .6 per cent.

The Incidence of Massive Collapse as an Association with Foreign-body Inhalation.—One can best quote in this connection the words of Chevalier Jackson in his remarks before the American Surgical Association in Washington, May, 1925: "We have seen at the bronchoscopic clinic, hundreds of cases of atelectasis affecting one or more lobes and often an entire lung. These cases have nearly all been due to bronchial obstruction." Save for the references to bronchial obstruction in the discussion on the etiology of massive collapse, it has seemed wise in this paper to leave the description of foreign-body collapse to those most familiar with the accident, and the reader is referred to the numerous contributions of Jackson and his collaborators. It need only be said that the result of their labors has been to prove conclusively that massive collapse of the lung is a well-established clinical entity.

Anatomical Findings and Conditions.—Complete carnification of patchy distribution has long been described in connection with lobular pneumonia, with abscess of the lung, with pleural and pericardial effusions; all post-mortem records include instances of more massive collapse of large areas or of a whole lobe seen as an unlooked for happening or finding in the autopsies on cases of pericarditis with effusion, of lobar or lobular pneumonias; a massive collapse has occasionally been revealed as complicating a large embolic infarction; it is probably correct to say, however, that the acute lobar collapse which this paper is considering is distinguished from other types of atelectasis by the absence of evidence in the collapsed area of bronchial obstruction, of inflammatory lesions or of embolic accident.‡

‡ The autopsy description given by Chevalier Jackson in the *Annals of Surgery*, Sept., 1925, differs very materially from that of other writers who describe acute massive collapse from the post-mortem side. In this case there is very evidently "bronchitis, bronchiolar pneumonia with atelectasis," an "exudate rich in fibrin, in the meshes of which are closely packed polymorphonuclear leukocytes." The question of a preceding infection with an *ensuing* collapse must be considered. In Wookey's case of acute collapse, with death in a few minutes (see page 142) there is naturally no inflammatory reaction; Bradford failed to find obstructing mucus or secretion, Hirschbroek's case showed but little sign of excessive secretion. The absence of retained blood in the air passages was a noteworthy feature of the "wounds of the chest cases." There are doubtless many causes for the same condition, but, as mentioned in the section on etiology, we rarely have the opportunity of seeing an autopsy on an acute case of collapse while the process is in course of development.

Little can be added to the descriptions of Pasteur, Bradford, Hirschbroek and others who have in their pictures detailed the absolute atelectasis of the lung and the absence of signs of contributory causes. Figs. 1 and 2 (case of Doctor Wookey, Toronto General Hospital) show how rapidly complete may be the collapse when evident obstruction has occurred; it is remarkable, however, if obstruction alone may cause a massive collapse, that the numerous cases of strangulation do not contribute more instances of acute atelectasis; an obstruction in the air passages, irritating the mucous membrane while acting like a ball valve, may perhaps produce a local bronchospasm and collapse of the lung beyond, as a result of both obstruction and reflex nervous action. Fatal cases of massive collapse of the lungs have shown nothing more than had been suggested by the examinations, sinking in of the ribs on the affected side, elevation of the diaphragm on the side of the collapse, swinging over of the mediastinum into the collapsed lung; no note is made as to whether marked distention of the great veins or auricles had occurred, such a happening might take place to relieve the acutely developing negative pressure in the thorax; small amounts of fluid have been found in the chest in some cases, this may help explain the very dense shadow of the affected side as shown in the X-ray pictures, and Leopold suggests that a pulmonary oedema, "a drowned lung," may be responsible for this unusual degree of shadowing. Lobular pneumonia affecting other areas of the lungs and of a later period of development has been the cause of death in several recorded cases; Hirschbroek details one autopsy revealing massive collapse of both lower lobes; bilateral involvement is, however, unusual. Without the complication of preceding lung disease, of abdominal operation, of chest wound or of ensuing lobular pneumonia, it is unlikely that a massive collapse will have a fatal ending. The histological picture gives no suggestion that would indicate vital changes in the tissue structure, if the tissue examined has come from a case in which early death was a feature. §

Etiology.—All attempts at explaining massive collapse of the lungs as something produced by a visible and recognizable agent are handicapped by the fact that there are as yet no autopsy records, save those which deal with foreign bodies in the air passages, *which show*

§ See the description of the histology of the lung in Fig. 2.

us the condition in the early hours or minutes of its production. The most complete examples of massive collapse of the lungs are those in which sudden blocking of trachea or bronchi has occurred; the case of Doctor Wookey above referred to is of greatest value in this connection for it records a complete bilateral collapse as a result of inhalation of food matters into the air passages; since death was a matter of a few minutes only, there was but little time for the absorption of the imprisoned air by the blood stream; something, therefore, must have contributed to the production of the absolute atelectasis. There are many suggestions, but all are lacking in an ability to prove that they alone can cause a massive collapse.

The condition of the affected lung is, of course, practically that of foetal atelectasis; since our lungs went at once from a condition of complete collapse, or non-expansion, to a state of expansion, with our first efforts of breathing, and since with this transition went hand in hand sinking of the diaphragm, lifting of the ribs, fixing in an elevated position of the upper ribs, it is possible that a mechanism exists by which, in unusual accidents, the upper ribs fall, the lower ribs droop and the diaphragm rises flaccid, as a result of a reflex paralysis, a resemblance to such a reflex action is occasionally in evidence in severe cases of angina pectoris, where in addition to the pain in the arm the ulnar muscles become paretic and wasted or subject to spasmodic movements. The diaphragm on the affected side has been watched in its lack of action, X-rays show it to be high, fixed, and its excursion greatly limited, or even stopped (Scott); pictures of the chest show that in many instances the ribs have dropped to their original foetal position. The known facts are that blocking of the air passages has produced quick collapse of the lung,¹⁷ which in some instances of bilateral involvement has ended fatally and that, in the less serious types, a paralytic condition of the diaphragm and a sinking of the ribs can be demonstrated. Whether it is permissible to suggest that an irritation, an obstruction in the lower air passages may be followed by or may induce a reflex paresis of the muscles of respiration, which with the absorption of the air in the lung beyond the obstruction, aids in the production of the active pulmonary collapse is dependent, of course, upon the admission by physiologists that there are such reflexes.

Pasteur considered, as did Pearson Irvine, that the massive col-

lapse they had seen in cases of diphtheria was due to paralysis of the diaphragm; there would always be the probability in these types of collapse that a lobular pneumonia with abundant secretion, and the aspiration possibilities of palatal paralysis, had contributed an irritant or obstructive detail to the condition; Rose Bradford in his papers upon infective polyneuritis states that he found instances of massive collapse of the lung associated with the paralysis of the diaphragm which was a feature of some of the acute cases; these cases were usually diagnosed pneumonia, though it is probable that the lobular pneumonia found existing coincident with the collapse was a late development and the result of aspiration. The contributions of Pasteur and Bradford suggest that paralysis of muscles necessary to respiration plays an important part in the causation of the massive collapse noted in their diphtheria and polyneuritis cases, respectively; this element, however, only comes into play as a secondary factor in the active lobar collapse seen as a post-operative complication, as a feature of chest wounds or as an associate of acute pulmonary infections, in fact would appear to exist as a result of the collapse and in order to help relieve the extreme degree of negative pressure which is developing perhaps with great rapidity; even at that, however, this demonstrable paralysis of the diaphragm has all the appearance of an acute reflex phenomenon; the same may be said of the sinking-in of the chest which makes a picture not imitated by any other pulmonary disorder. In early discussions there was spoken of as possible an active lobar collapse, which in its production threw the muscles of respiration into inactivity and induced the sinking of the chest wall and the rising of the diaphragm to accommodate itself; like the reflex above suggested, however, this assumes the existence of physiological activities which are as yet not known, and one must turn to the region of greater probabilities.

The reports from bronchoscopic clinics, cases such as those detailed from the experiences of St. Clair Thompson and Wookey, the experimental work of Lichtheim, all indicate that bronchial obstruction, either of acute or chronic nature, may produce a massive collapse of the lung; it must always be suspected that the acute massive collapse occurring suddenly in the course of a pneumonia or pleural effusion results from obstruction, either a plugging with sticky exudate or an occlusion brought about by a swelling of the bronchial

mucous membrane; in chest wounds penetrating the lung there will have been both blood and exudate in the bronchial tree; in the post-operative massive collapse there will have occurred inhalation of secretions and irritation of the lung by the anæsthetic; temperature reactions and expectoration suggest that in the latter group of cases, infection of bronchi and bronchioles is a contributing factor. If one remembers that the typical end-result of pneumonia, pleurisy or disease of the lung is an evident lagging and disinclination of the respiratory muscles of the affected side to do their work (Warren Coleman) then the sequence of events in some cases of collapse would be—bronchial obstruction, absorption of air in the lung beyond, tendency to collapse, not only unopposed by the respiratory efforts but actually encouraged by them; in the sinking of the ribs the rising of the diaphragm is a relieving compensating process, and the absence of signs of muscular activity suggests that it is something not to be actively combated.

In all this etiological uncertainty, one important clinical detail should be borne in mind; many reports speak of the over-distention of the lung on the side away from the collapse, this distention has in some instances given rise to the diagnosis of an acute pneumothorax, though more careful examination showed that this condition was not present; an acute emphysema must nevertheless have existed and if the greater part of one lung was progressively collapsing, it would be reasonable to suppose that this acute unilateral emphysema unopposed by solid lung or fluid on the other side will have a distinct influence in displacing the mediastinum and heart and allowing the process of collapse to continue. Acute emphysema of the lung on one side, such as one might see as a compensatory process in pneumonia or pleurisy with effusion, could not perhaps displace a heart and the mediastinal partition into solid lung or fluid, but opposed only by a retracting lung and possibly aided by a certain degree of negative pressure on the collapsed side it may play a large part in producing the characteristic physical signs and findings; a study of the intra-thoracic pressure on the emphysematous side may give much needed information. Some few reports deal with massive collapse as occurring subsequent to operations and wounds away from the chest or abdomen, it has also been reported as an incident of surgical procedures conducted under local anæsthesia; in none of these

reported instances has there been considered the possibility of a pulmonary embolism from lacerated and thrombosed vessels in the wound site. We have no descriptions of active massive collapse occurring as a part of the embolic accident, it must be considered, however, as a matter of course, if we attribute to irritant causes the ability to provoke certain pulmonary reactions and at the meeting of the Association of American Physicians in 1923, it was stated in the discussion upon a paper dealing with massive collapse, that one observer had seen his first instance of the condition within a matter of a few days and that the collapse was associated with pulmonary embolism. That embolism may occur in the form of showers of minute thrombi from the field of operation even in the early minutes of the performance and may constitute a very possible source of pulmonary irritation leading to acute pleurisies, or to lobular pneumonias about the numerous small infarcts, is an idea put forward at present by all who are concerned in investigating the causes of post-operative pulmonary complications.¹⁸ It is hardly to be gainsaid that, if the irritant emboli can excite such changes as just mentioned, the assuming of the contribution of the anæsthetic and inhaled secretions to the production of these pulmonary lesions is unnecessary, and further, that if multiple emboli may come from any large wound whether in the trunk or extremities, then any surgical procedure with or without general anæsthesia may be followed by active embolic lesions which in turn may, in suitable subjects, provoke an acute massive collapse of the lung.

What may be the factors in the producing of a so-called "contralateral collapse," the collapse of the unwounded lung in cases of chest wounds, a condition with which we became familiar in our war-wound experience, is difficult to say; those who assume a reflex causation of massive collapse see in this form of the accident the most convincing argument in support of their claim; Bradford speaks of acute massive collapse of the lung on one side with a simple graze wound of the ribs on the other. In one of the cases which came to light in an analysis of three years' post-operative pulmonary complications, the resection of a small rib tumor on the right side collapsed the base of the lung on the left; as a general anæsthetic had been used, however, irritation from within must be held to have contributed. It should be remembered in considering superficial wounds—or

traumata of bones and ribs as possible causes of collapse—that fat embolism may have occurred to irritate the lung; the curious condition spoken of as the “pleural reflex” indicates that there are, moreover, nervous mechanisms in the pleura which are by no means understood and which under certain circumstances may assume unlooked for activities.||

The Clinical Picture of Massive Collapse.—Occurring in the course of a pericardial effusion of an acute pulmonary inflammation or a pleural effusion, a massive collapse often appears as an alarming complication in which the sudden urgent dyspnoea and signs of dissolution suggest an attack of heart failure or some such conditions as actively spreading infection, rapid accumulation of fluid, infarction, or perhaps embolism from some unknown source. The dyspnoea may be intense, the pulse-rate rises rapidly if not already high; in one of our early cases the prostration was extreme; it is probable that in some cases a massive collapse may develop in an insidious manner without urgency and that in many pneumonias and pleural effusions, rapid extension of areas of consolidation or the suggestion of quick outpouring of fluid without added distress, may mean collapse rather than spreading infection and increasing amount of exudate; it is not to be doubted that a massive collapse is a much more frequent accompaniment of acute thoracic disorders than has hitherto been suspected. The more slowly developing collapse of the bases in asthenic conditions and of the left base in pericardial effusions has, however, long been recognized; these conditions are often seen to progress in an almost symptomless manner. The intensifying of the dyspnoea was the main feature in three instances of acute massive collapse complicating pneumonia; fever, increase of expectoration and cough were already in evidence, there was no pleural pain; after a few hours of urgent symptoms, two affected upper lobes re-expanded and the patients became comfortable; in the third case the collapse of the lower

|| In the etiology of “foreign-body collapse,” Jackson reverts to the old ball-valve theory of Gairdner (“Bronchitis,” 1850). A plug of thick secretion is drawn further into the bronchiole with each inspiration; it finally comes to rest and blocks the passage; air no longer can enter, but expiration can still force some air out; the blood absorbs the residue of air in the lung beyond the obstruction and the lung collapses. Conversely a plug may be so situated that air may enter the lung sac but is not easily expelled; an emphysema of localized character will result.

lobe and the sinking-in of the lower ribs remained in evidence for some days.

Complicating a surgical operation the stormy course of acute massive collapse of the lung is a matter of the greatest clinical interest. An abdominal section is the usual preceding history, one of Scott's forty collected cases was preceded by a hemorrhoidectomy; it will probably be found that a collapse may ensue upon any surgical operative performance on the periphery, thrombo-embolism or fat embolism being the exciting or contributory cause; four cases in my own experience followed close on appendectomy; a case of more recent date in the service of Dr. G. E. Wilson, of the Toronto General Hospital staff, occurred after opening the abdomen for the relief of a suppurating appendix. General anæsthesia has been given in the vast majority of cases, the instances of collapse reported by Elliott and Dingley, however, include the description of a massive collapse of complete degree, subsequent to a spinal anæsthesia, the frequent occurrence of the condition in association with wounds of the chest indicates that anæsthesia and previous or existing infections in the air passages play little part in the production of this traumatic type of the lesion.

Following the operation, usually within seventy-two hours, sometimes almost before the patient has recovered from the anæsthetic, the active symptoms of respiratory distress—dyspnœa, chest oppression, pain(?), irritating cough, and perhaps some mucoid expectoration—are noted; the temperature may or may not be elevated, in Leopold's four cases the maximum temperature was 99^2 in one instance, and below 98^2 in the other three; in Scott's cases 100^2 , 99^8 , 99^0 , 98^8 were the highest temperatures recorded; one of Hirschbroek's post-operative massive pulmonary collapse cases ran an afebrile course, my own examples of the condition showed a greater range of temperature with the acute symptoms, but like other post-operative complications, massive collapse may take place during the febrile period of the surgical disorder; there is much evidence in these reports of Scott, Hirschbroek and Leopold to indicate that in many instances the infection of the respiratory tract has little to do with acute post-operative pulmonary atelectasis. The acute respiratory distress, so acute that the diagnosis of pulmonary embolism will often be suggested, tends to pass off in a few hours, in two of my

cases, developing within four to eight hours after the operation, it had been reported that they were so strenuously oppressed that death must ensue; on the other hand, the development of massive collapse may be quiet enough to be called latent; with the rapid labored respiration of such sudden onset may be seen a heart-rate high enough to make the consideration of tachycardias or heart flutter a possibility; cyanosis of a marked degree may develop as the collapse progresses, only to disappear as the chest accommodates itself to the new conditions. The cough, expectoration and pain in the chest are best described as uncertain associations; the first of these symptoms may often be strikingly absent if there is no secretion, or be but a happening of the first few hours; expectoration may be absent, it may be of a mucoid character, it may be blood stained, in which case embolism must be thought of as a possible incitant of the collapse (Scrimger); if the pain complained of is sharp and in its character suggestive of pleural pain, embolism is again to be thought of, for there is nothing in the development of a massive collapse which should incite a lesion of an inflammatory nature; pain in the chest at the third left costal cartilage was a symptom in one of the fatal pulmonary embolisms tabulated from the surgical service of the Toronto General Hospital; in one of my cases of massive collapse, pain was complained of on the side of the developing collapse, there was no pleural rub; in the other cases præcordial distress rather than pain was the feature of the onset; Scott mentions pain as having been present in one-half the instances of massive collapse which he has analyzed; there is, however, no detail as to the nature of the painful sensations complained of. Neither expectoration nor cough was a feature of my own cases. The pulse-rate rises rapidly in urgent cases. With the passing-off of the acute distress in the matter of a few hours, the patient acquires a degree of relief and by the next day may show no trace of the active symptoms, though the physical signs may remain unchanged; it has been noted in many of the cases that for a period of even two weeks the collapse may seem to partly disappear only to re-appear in the course of a few hours, the early distress, however, is never imitated in these recurrences. Lobular pneumonia follows the collapse in many instances and must usually be held responsible for the rising temperature and pulse-rate, with sputum and cough; whether the beginning of the lobular pneumonia is signalized by the appearance of the massive

collapse in some patients or whether the collapse induces or favors the development of an infection is a question yet to be answered; an uncomplicated massive collapse may be fever free in one or two days, Scott's tables give the details of the duration of both physical conditions and febrile reactions. Urgent as are the symptoms of acute post-operative massive collapse, yet the accident is rarely fatal; of the forty collected cases in Scott's report, thirty-nine recovered; the fatality showed a condition of bilateral collapse affecting both lower lobes.

As an accident happening subsequent to a wound in the chest, massive collapse had a ready recognition during the great war, and observers had but little difficulty in collecting the interesting details; the acute symptoms and the remarkable physical signs, together with the knowledge that a missile had penetrated the chest, going perhaps in a direction which seemed to indicate that both lungs and both pleural cavities had been opened, created many difficulties, and the acute urgencies were often ascribed to causes other than the evident collapse; with a unilateral wound and collapse, if the displacement of the heart was not noticed, it was common to find that the urgency with the signs of a full chest was considered as due to rapid increase of blood in the pleura with increasing intra-thoracic pressure, and unnecessary attempts at aspiration, which produced perhaps but a few drams of blood, were often made; the amazing improvement of these patients by the next morning was a feature of every "chest-wound service"; an unfortunate detail of these unilateral wounds with collapse of the wounded lung was that at times the over-distention and the hyperresonance of the sound and compensating side would provoke the diagnosis of pneumothorax and lead to puncturing of the chest in the vain hope of removing free air; the discovery that the unwounded lung was subject to the accident of collapse is of interest, as already noted, because it depreciates the influence of infection and the general anæsthetic as prime causes of massive collapse in the post-operative cases, it does not, however, interfere with the idea that the introduction of foreign material into the air passages may be an active contributory agent, for in a chest wound there is rapid flooding of the air passages with each inspiration, if the bleeding is free; it is extremely difficult to explain this contralateral collapse on any other basis than that of obstruction, irritation and a

response to this irritation in the rising of the diaphragm and the falling-in of the ribs to compensate for the collapsing lung. With a contralateral collapse well established, the fact was often noted that the motionless, flat side with its hidden sounds was accused of harboring blood or fluid in quantities and of causing the gathering distress; with high fever and infection existing as a result of conditions on the wounded side it occasionally happened in times of stress that the chest was opened on the collapsed half, looking for collections of blood or pus. In general, however, the symptoms of massive collapse as complicating a wound of the chest are those of the collapse seen in the post-operative period. The remarkable resisting powers of the human frame are nowhere better seen than in these collapse cases complicating the wounds of the chest. Fig. 9, from a man who recovered after a few hours of urgency, shows that, in addition to the complete and solid collapse of the unwounded side, the aerated area of the wounded side is almost half obliterated by effused blood and associated atelectasis or infarction.

The Physical Signs of Acute Massive Collapse of the Lungs.—Save in the slowly developing latent type of cases, orthopnœa and cyanosis are strongly in evidence; the labored breathing may reach a rate of 50 to 60 per minute; the rapid rise of the pulse-rate to 120 or 160 with the dyspnœa and cyanosis of sudden development, gives the picture which might be drawn to represent any of the acute heart failures, pulmonary embolism, pulmonary œdema or rapidly developing pneumothorax. In a typical case of massive collapse of the apex, it will be noticed that the interspaces have fallen in and that the upper chest seems to have shrunk and is almost motionless as far as true expansion is concerned; if the expansion of the unaffected side has reached the degree of compensation sometimes acquired, this side may seem full enough and hyperresonant enough to suggest to the casual observer a pneumothorax; if the collapse of the right side is complete, the heart may be seen beating to the right of the sternum, in collapse of the left apex the heart rises high and with collapse of the left base the heart-beats may be felt in the axilla; an X-ray plate of the chest gives a remarkable picture if taken in the early hours. In many of these plates it is seen that the collapse on the right side has drawn the heart shadow away from its position on the left side and it has disappeared into the dense shadow of the collapsed lung, or with

collapse of the left lung the right heart border is noted as not projecting beyond the midline to the right; the condition is something quite unlike that produced by either consolidation of the lung, or by effusions into the chest, as the displacement of the mediastinum is always toward the affected side. The pictures of the early days show frequently that the diaphragm has risen in the chest and is motionless as if in a state of paralysis; at times there is evident a distinct falling in and down of the ribs, suggesting that the accessory muscles of respiration are also in a paretic state; in many instances the density of the shadow in the chest is that of fluid and it is possible that there may be some outpouring into the pleural cavity in the early hours of distress, in order to attempt help neutralize the rapidly developing negative pressure; the over-expansion of the unaffected side may be indicated in the plates. If the chest is examined from day to day by means of the X-ray, it can often be seen that the density of the collapse may vary considerably, and it appears that a relapse to the conditions of the early hours is not unusual; clearing is a gradual process which requires in some cases as many as ten to fourteen days; the heart is gradually replaced; plates in some instances have shown that the expansion of the lung is earliest in evidence at the periphery. As yet there are few notes from the X-ray studies indicating that effusions or abscess may complicate a massive collapse.¶

Confirming the inspection, one notes readily by palpation the difference in movement of the two sides of the chest; there is no pulmonary condition with which we have familiarized ourselves in the past, which shows the same remarkable limitation in movement as massive collapse; vocal fremitus may or may not come through; with a plug in the bronchus the vibrations may be checked, but, on the other hand, a collapsed lung is a consolidated mass, and may conduct readily both fremitus and sounds; percussion over a collapsed lung gives usually a toneless note, a lack of resonance which from being complete in the early days and hours will vary as the lung begins to expand and be replaced by a note of modified resonance, by wooden tympany and finally by resonance; the feeling of solid resistance is very definite; the auscultatory phenomena have a wide range, from absence of sounds to tubular and amphoric breathing; in collapse

¶ The recent paper by Scott described a pleural effusion ensuing upon a collapse.

from obstruction it is usual to note hidden sounds, but here again, as in the question of fremitus, one remembers that a collapsed lung is a consolidated body and may transmit readily, in my own cases tubular breathing was the more common finding, though one often noted that the tubular breathing of one day might be superseded by a period of absent breath sounds on another.** Râles were not a feature of the early hours in my cases, though as the lung began to expand showers of crepitant râles could be heard with inspiration; in the experiences of others, sounds indicative of moisture were usual; in those cases in which signs and symptoms of spreading infection supervened upon the collapse while the lung was expanding, it has been the observation that moist râles were in evidence; it must be obvious, however, that a completely collapsed lung is not in a condition to produce râles, however well it may conduct sounds. There have been no other adventitious sounds made note of; it is of interest that, though chest pain has been frequently recorded, no signs of pleural irritation have been found.†† The heart has shown no peculiarities.

Differential Diagnosis of Massive Collapse from Other Intra-thoracic Conditions.—In the slowly developing examples of collapse of the lung as seen in asthenic individuals or in a case of pericardial effusion (perhaps the best known examples) one's attention has already been drawn to the area of lack of resonance, of hidden sounds or even of increased and tubular breath sounds at the bases of the lungs; consolidation or fluid is usually suspected and the needle must often be used to make determination absolute; perhaps from lack of observation, displacement of the heart and mediastinum has not seemed to be a striking feature of these conditions and it is evident as concerns pericardial effusion that a full pericardial sac, stretching to the right, might interfere with a reading of displacement while yet the mediastinum was drawn to the left to an appreciable degree;

** An interesting auscultatory and percutory phenomenon may be referred to; Fig. 5 shows well the collapse at a depth, with aërated and resonant lung overlying; light percussion may not suggest the condition existent deep in, heavy percussion will bring out the impaired resonance; through the thin layer of expanding resonant lung the voice and breath sounds may be heard as amphoric, bronchophonic or tubular; one is reminded of the deep-seated bronchophony which may be heard under the resonant lung of the sound side, when by displacement of the trachea and bronchi as a result of complete thoracoplasty, the air passages are so placed that their sounding qualities come through to the ear.

†† Cf., however, the statements of Jackson, *loc. cit.*

careful X-ray studies and the use of the needle are frequently necessary to make clear the nature of the area of lack of resonance which abuts upon a large effusion into the pericardium. Collapse should always be suspected, it is the common associate of pericardial effusion. When in the course of an acute thoracic condition the patient is suddenly seized with intense dyspnœa, with rapidly deepening cyanosis, with chest oppression, cough and fluttering pulse, the suggestion is ordinarily made that increasing infection, spread of consolidation, outpouring of fluid into the pleural cavity has taken place, or that a heart weakness due to muscle failure is developing; an increase in the area of dulness, a slight rise in the temperature seems to confirm the diagnosis and if the heart area is not carefully delimited, collapse of the lung will not be suspected; with recovery from the shock the physical condition may be apparent; in a pneumonia the newly affected area is seen to be depressed, and though the signs may be those of fluid or consolidation, yet the sinking of the chest and the evident displacement of the heart into the newly developed area of dulness should at once give the suggestion of the true condition. In pleural effusions the acute collapse can of course be most easily appreciated by realizing that with the apparent increase of exudate which has suddenly occupied the apical area there is retraction of the spaces and perhaps return of the heart already displaced by the effusion; the signs over the upper part of the lung may be more those of consolidation than of fluid; comparison with a previous picture might show that the diaphragm had risen to a higher position than that occupied in the earlier days of the effusion.

It is probable that acute collapse of a lung lobe as a complication in the course of a pneumonia has been under our eyes from all times; in two cases of this sort which came to notice amongst six hundred of the pneumonia patients in the Philadelphia General Hospital, the resolution was a matter of a few hours; with one's attention taken up in the relief of symptoms which most often would be ascribed to the threatening heart failure, it can safely be said that many instances of collapse of the lung, as an incident in thoracic affections, have run their course before an interested observer has had the opportunity to check accurately the physical conditions in the chest. The diagnosis will be rarely in doubt when the accident takes place in the course of thoracic diseases and infections, if one remembers that

a pulmonary embolism is unusual in these cases since there is not often a phlebitis in evidence or existence; that neither an infarction, an increase in the area of consolidation, a pulmonary oedema, an extra outpouring of fluid, an acute pleural pain nor the various forms of heart failures will produce an area of impaired resonance into which the heart or its shadow can be seen to be drawn. The rapid heart action and breathlessness will inevitably suggest heart failure unless the area of collapse and the mediastinal shifting are observed. It is unlikely to a degree that a pneumonia would spread so quickly as to involve an area as large as is represented by the collapse of a lung lobe within a matter of minutes, yet one feels that the diagnosis between massive collapse and a spreading pneumonia has often failed in the making because this point has been overlooked.

The Diagnosis of Massive Collapse after Operation from Other Known Post-operative Cardio-respiratory Accidents.—The acute "pneumonias" of the post-operative period are lobular pneumonias if related to the operation, and are bilateral in their distribution; like a collapse they belong to the first seventy-two hours of the convalescence; they show a rapid onset with high fever but lack the element of acute shock which distinguishes most of the cases of acute atelectasis; they show no displacement of the chest structures and an X-ray would reveal no rising and paresis of the diaphragm; this position of the diaphragm might be the only distinguishing feature of a bilateral massive collapse of the lungs, such as existed in the case of Hirschbroek's; from a unilateral consolidation sometimes apparent when a post-operative lobular pneumonia is perhaps more outspoken on one side than another, or when, as might happen, a surgical convalescent has developed an infectious lobar pneumonia, collapse would be distinguished by its ability to draw over to itself the mediastinal partition; one never as yet seems to have had to diagnose a rapidly occurring collapse of the lung after operation from large serous or purulent effusions; these conditions as a post-operative happening rarely take place apart from abscess, septic pneumonias or infarcts; in clean surgical performances one does not expect to see exudation into the pleura; the effusions will lack the stormy onset of the collapse and will displace the mediastinum away from their place of occupation. It must, of course, be remembered as detailed in the description of massive collapse occurring in association with

the acute affections of the chest, that with the development of an acute collapse of the hitherto expanded upper lobe in a case of pleural effusion the already displaced mediastinum may swing back and produce the unusual appearance of pleural effusion without organ displacement. In wounds of the chest with hemothorax, and collapse of the wounded lung, lack of displacement of the heart, or, even, if the collapse outweighed the effusion, drawing of the heart into the side of the hemothorax was a condition often met with. Fat embolism with its bilateral manifestations of diffuse lobular pneumonia should not give a picture likely to be confused with massive collapse. A slowly developing collapse of the base, not unusual after a long post-operative convalescence, has little to distinguish it from an effusion or consolidation unless there is a displacement of the mediastinum in evidence; its latency, the absence of distinct febrile reaction and the very active evidence of mediastinal displacement should warn the observer that the condition found is not a simple pneumonic infection of low grade. The usual differential signs may not be of great aid, for it is common enough to have at different times in the same example of massive collapse, absent vocal fremitus, distant, hidden or absent breath sounds, diminished or absent voice sounds or, on the other hand, increased fremitus, increased and tubular breath sounds with perhaps bronchophony and pectoriloquy; the aspirating needle, the tests for movement of fluid within the chest, or even the taking of an X-ray picture, may be necessary in order to arrive at correct conclusions. Massive collapse of the lung subsequent to operation has probably escaped observation for so many years for the reason that its acute symptoms have been regularly confused with those of pulmonary embolism, which, of course, is most commonly seen after abdominal operations and their thrombophlebitic complications; the onset of both collapse and embolism may be dramatically sudden; the distress and dyspnoea may be of equal degree; the mere fact that life persists after the first shock may be the indication that something other than embolism has happened, though one is familiar with the fact that pulmonary emboli are by no means always death producing, and that death from embolism may be a matter of hours. Sudden distress after operation, cyanosis, acute pleural pain, with or without bloody sputum, a pleural rub with or without an evident area of consolidation, recovery, is the

picture of the so-called "minor" embolism¹⁹ and if there is a phlebitis in evidence there should be no doubt as to the diagnosis²⁰; if the picture be so altered that acute pleural pain, bloody sputum and pleural rub be omitted, and if it be indicated that into a very large and evident area of consolidation there has suddenly swung over the heart and mediastinum with an accompanying sinking-in of ribs and chest wall, then the occurrence of a massive collapse should be suspected, for embolism should not displace the chest contents either away from or into the affected area. Recovery from the early urgencies of both these acute and alarming conditions will allow readjustment of diagnosis made often under great difficulty, and the striking physical characteristics of massive collapse will then speak for themselves. The large, rapidly fatal emboli rarely allow symptoms other than distress or cyanosis to develop, a turmoil of sounds and râles may be the sole findings; even should a large infarction develop by reason of the embolus not killing and be able to produce the signs of a consolidation, it will not displace the mediastinum, nor give the suggestive signs of the massive collapse. As regards the diagnosis of massive collapse from certain cardiac accidents, it can be said that it will only be in the early minutes of the distress that a massive collapse can be confused with the acute heart failures of different natures; the tendency to the postponing of the fatal issue becomes evident and an examination made with the patient in a state of comparative comfort shows the beginning or establishment of the lung collapse, with the dislodging of the heart from its normal position; a rapidly forming infarction of the lung, in a surgical case who had a heart weakness, might lead to a momentary difficulty in diagnosis; the bloody sputum of the infarct should attract attention, and though the infarction be large the absence of mediastinal displacement would let the examiner know that the consolidated area was not collapsed lung. The distention and hyperresonance of the unaffected and compensating lung should not mislead the examiner into believing that a pneumothorax has taken place.

The Diagnosis of Massive Collapse from Other Thoracic Complications Occurring after a Wound of the Chest or Lung.—In the "chest-wound services" of the war of 1914–1918 one noted that a unilateral wound of the chest wall or of the lung in which there was little or no laceration was frequently found to be associated with an

urgency out of proportion with the damage inflicted, or to the slight degree of hemoptysis; with the urgency a consolidation of the lung area much greater than was to be expected from a slight trauma was at times in evidence; a massive hemothorax was usually suspected, but attempts to relieve the condition by aspiration of effused blood supposed to be present in the pleura, failed by reason of the finding that the chest condition was one of consolidation of the lung due to collapse of either the whole organ or the undamaged part, the wounded area of the lung being in a state of solid infarction, and airless; it soon became known in the medical services that in cases of this sort, sinking of the chest and interspaces, rising of the diaphragm on the side of the chest wound, airless state of the lung with displacement of the mediastinum into the consolidation meant massive collapse of the lung with or without hemothorax. The sinking of the chest on the wounded side and the over-expansion of the unwounded compensating side, plus the position of the diaphragm and mediastinum, if an X-ray picture could be procured, were the suggestive diagnostic points. The rapidity of the appearance of the consolidation and the absence of any distinct degree of fever had often given rise to the suspicion that some condition other than infection, pneumonia, or effusion, was existing.

In the cases where, from unexplained causes, the massive collapse affected suddenly the lung on the unwounded side, it was often suspected that the missile had gone into and damaged the sound lung, causing another but larger acute hemothorax; attempts at aspiration were frequently made, but of course with negative results. With the recognition of the condition present, the diagnosis could usually be made by observing the position in the consolidation of the mediastinum and heart, drawn much further over to the side of the collapsed lung than was usual when a small hemothorax was present on the wounded side and was allowing the mediastinum to be slightly displaced; if, as happened in the earlier days of the war, there might not be an X-ray plant at hand, it must sometimes have happened that the collapsed side was opened surgically under the impression that the relatively clear chest on the wounded side was not responsible for the urgent symptoms.††

†† On two occasions the writer saw wounded men removed from the operating room whither they had been taken to have the solid chest explored.

Instances of collapse of the lung in association with wounds of the chest are not likely to be met with, with any degree of frequency, in civil practice; the accident surgeon, however, should realize that, either on the wounded or unwounded side, a massive collapse may occur; if the associated accident is on the side of the wound the heart and mediastinum will displace themselves into the damaged side, if, however, it is of the "contralateral type," that is, on the side away from the wound, his diagnosis of the conditions present will depend on his ascertaining the course of the missile and its position, and the recognition of the fact that the solidly contracted and consolidated chest, instead of pushing the mediastinum away (as would an effusion of such bulk), has drawn it into itself.

The Prognosis of Massive Collapse of the Lungs.—Recovery is the usual termination of an uncomplicated unilateral massive collapse, such as is seen in the post-operative cases, a lobular pneumonia of later development may affect the issue unfavorably. A bilateral collapse of the bases only might allow recovery. §§

As far as is known from observation of clinical cases, the collapse ensuing upon the various affections and infections of the chest is not apt to be the immediate cause of death, autopsy records of cases of massive collapse are few. |||

In the desperate "chest-wound" cases one felt that the added collapse of the unwounded lung was often the definite cause of the fatal ending.

Treatment of Massive Collapse of the Lungs.—Foreign bodies in the air passages must be removed, Jackson details the removing of thick and tenacious secretions. If no urgency is in evidence and no foreign body present the lung can be left to look after itself; in the great majority of the cases, the use of large doses of morphine is imperative, oxygen might be freely given; as the lung is perhaps affected by pressure, in the instances where collapse is associated with pericardial effusion, change of position from recumbent to erect may help; removal of exudates, if present, should be done, tight binding of the chest or abdomen should be relieved.

§§ Hirschbroek's bilateral basal collapse ended fatally. In Jackson's case pregnancy and cesarian section preceded the fatally ending massive collapse.

||| The best example in my own collection of a collapse associated with lobular pneumonia at autopsy, showed involvement of the whole left lung and the right base in the infection, and collapse of the remaining unaffected right upper lobe.

ILLUSTRATIVE CASES; MASSIVE COLLAPSE COMPLICATING PNEUMONIA
OF THE RIGHT BASE

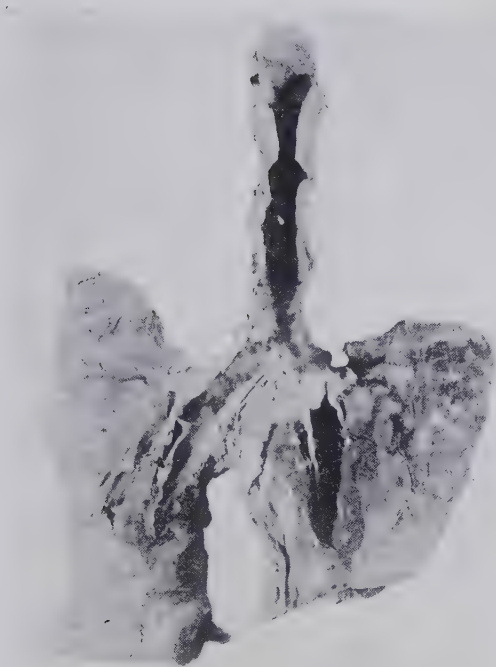
CASE I.—Woman, aged sixty. Complete consolidation of the right lower lobes; about the fifth day of the disease seized with a sudden attack of dyspnœa and prostration and she became cyanosed. The heart-rate was rapid when seen and a heart weakness was suspected; examination showed, however, that the upper lobe which formerly had been over-expanded was now sunken in and quite solid; the sounds and percussion findings suggested a new area of consolidation, but the rapidity of involvement seemed unusual; inspection revealed the fact that the heart was beating to the right of the sternum where it could be felt; there was no cardiac dullness to the left of the sternum; although we were not familiar with the condition of massive collapse at this time, yet the findings suggested this process of lung involvement more than a fresh pneumonia. In this case clearing began in six hours and the heart was replaced within a matter of three or four days.

CASE II.—Collapse of the left base with pneumonia. Patient entered hospital with signs of a small consolidation at the left base. During the night there occurred an attack of dyspnœa and in the morning the involvement seemed more extensive, with the added features that the apex beat was felt in the axilla and that the chest seemed collapsed; an X-ray picture gave the findings as depicted in Fig. 3; the falling of the ribs is seen to be extreme and the right side of the chest shows little sign of the right heart border. Improvement was rapid in this case also and the patient left hospital in a week with the heart and mediastinum restored to their position.

CASE III.—Pneumonia of the left base in a boy of six; involvement of the apex at the end of two weeks without any added distress; chest completely solid, sounds tubular, and varying from day to day there were notes that râles were or were not heard. Left chest sunken, motionless, right chest over-expanded but clear; no heart dullness to the right of sternum. Heart beating in the second and third interspaces, stomach tympany and diaphragm up to the third rib in front; the solidity of the lung behind was that of complete fibrosis or new growth. Puncture found no fluid. An examination three days later showed that resonance was appearing in the left mid-back and as he breathed deep the resonance could be noted as increasing and improving, the heart was lower in the chest: An X-ray revealed the fact that it was now in place and the diaphragm lower; six weeks were required for complete clearing of the lung in this case. No fluid found by X-ray; a case of this sort may explain some of the instances of non-resolution; fever kept up for the six weeks, there was but little cough and no expectoration.

CASE IV.—Pericarditis with effusion; collapse of the whole left lung. A woman of sixty-three years seized with fever, aching, and after a few days showing distinct pericardial friction and signs of distress; an effusion into the pericardium was looked for but not demonstrated; signs of a consolidation at the left base developed without fever; sudden onset of weakness, dyspnœa and signs of dissolution; on rallying it was found that the chest was now solidly dull, with tubular breathing overall and good fremitus; heart not found to the right and no differentiation could be made between heart and lung dullness on the left; diaphragm seems high; no fluid found on puncture; heart sounds best heard high

FIG. 1.



[Complete collapse of both lungs from impaction of food particles in bronchus.

FIG. 2.



Microscopical section of lungs pictured in Fig. 1.

FIG. 3.



Collapse of the left base in association with pneumonia. The deviation of the mediastinum and heart to the left is apparent, the remarkable degree of falling in of the chest and obliquity of the ribs which represents the attempt to compensate for the collapse is well shown. There is no scoliosis.

Fig. 4.



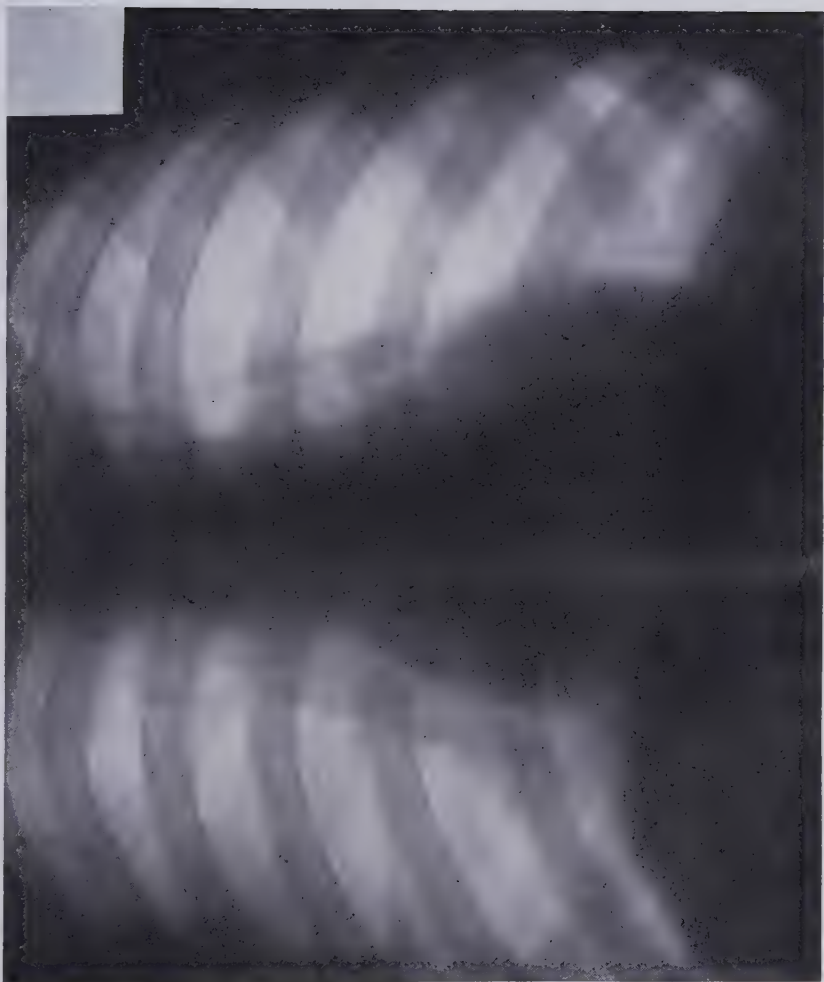
total collapse of the right lung as a post-operative accident; the heart has progressively disappeared into the right chest

FIG. 5.



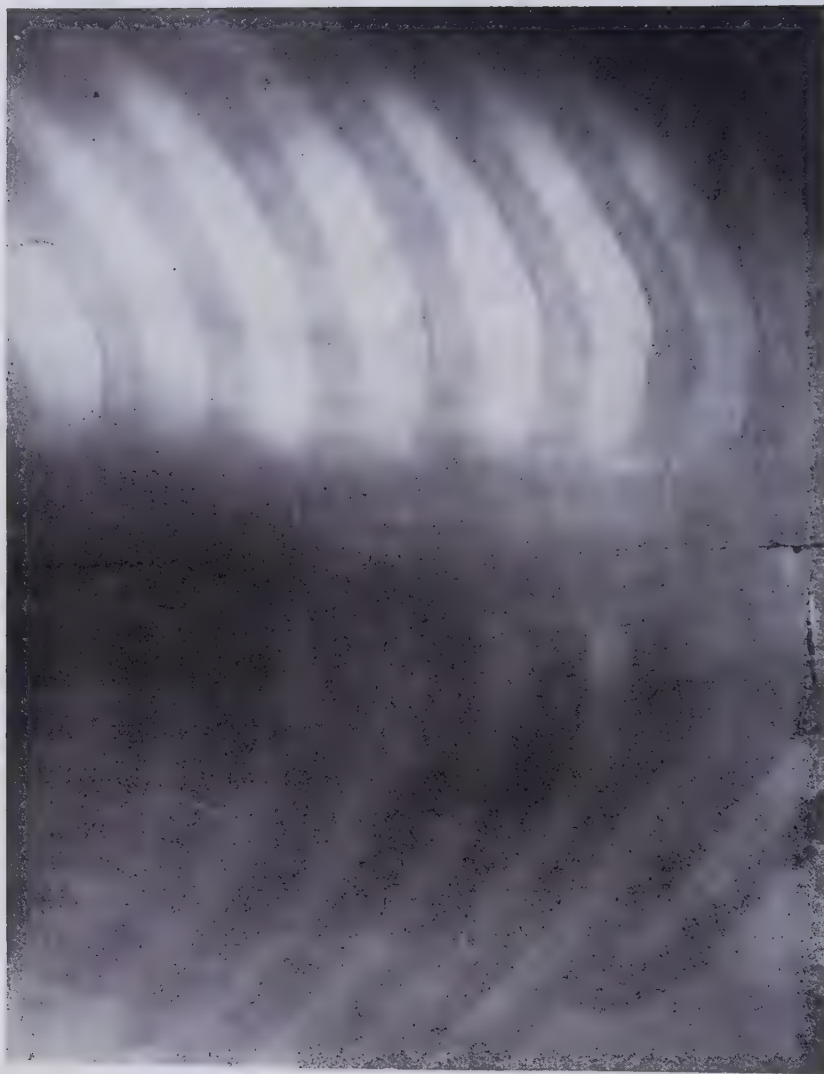
The collapse is beginning to disappear, expanding lung to the extreme right margin of remaining collapse, replacement of mediastinum.

Fig. 6.



Eventual replacement of mediastinum as lung clears, some signs of the collapse process still in evidence as diffuse shadows.

FIG. 7.



A very complete picture of acute massive collapse of the right lung after operation. The falling of the ribs is evident; the heart and mediastinum are completely displaced into the consolidation.

FIG. 8.



The same lung resolved; no full size plates were at hand at the time of taking these pictures;
the heart shadow is seen to the left.

FIG. 9.



This section of lung shows complete collapse of the alveoli in most of the section and partial collapse in the rest. The capillaries of the alveolar walls are all engorged with red blood-cells. There is no evidence of an inflammatory reaction. The bronchioles show a partial collapse and for the most part are filled with red blood-cells and a few wandering cells. The blood-vessels throughout appear normal.

in third and fourth spaces; the lungs gradually cleared. There could be noted in this case in the middle of the left back, as clearing went on, that on light percussion there was resonance, although the breath sounds were distinctly "distantly-tubular" and the voice sounds bronchophonic. It is probable in this case that the retraction of the pericardium into the collapsed lung eventually precluded the diagnosis of pericardial effusion: The early consolidation at the left base was very suggestive.

MASSIVE CONSOLIDATION SUBSEQUENT TO ABDOMINAL OPERATION

CASES V, VI, VII and VIII were all massive collapse subsequent to appendectomy, they were young men and with one exception were clear in their chest before operation, in only one of them was there perforation or pus collection; in all four ether was given and in all four the acute symptoms are indicative of the fact that the onset of massive collapse had begun well within twenty-four hours.

In one of the cases, seen with Doctor Coatsworth, of Toronto, the removal of a chronically thickened appendix was followed in twenty-four hours by rapid rise of the pulse-rate, slight temperature, and progressively urgent dyspnoea with cyanosis. The patient was found propped up in bed, badly cyanosed, sweating, and gasping for breath, *there was no acute pain*, but marked feeling of constriction in the upper chest, pulse was very rapid and weak, respiration 50; the right chest much fuller and moving much more than the left, this side of the chest was also hyperresonant and the sounds were distant, but vocal fremitus was present, there were no signs of free air in the pleura. The left chest was noted as retracted, moving little or not at all, percussion note everywhere much impaired and almost flat in the axilla. Note was much impaired over the whole back, vocal fremitus was present, sounds were everywhere distant, there were many crepitations heard. There was no heart dulness to the right of the sternum and it was lost on the left side into the dull area of the left axilla and apex, an impulse was felt in the second and third interspaces by the anterior axillary line. Six hours later, in the evening, the right side had lost the early suggestion of pneumothorax, the complete consolidation of the left side was more in evidence, vocal fremitus was present, no change in the breath sounds, he was bringing up a very thick sputum in which there was no sign of blood; improved by mid-night, pulse-rate fell rapidly, six days later there was only a small area in the left mid-back where there was distant tubular breathing with nasal voice sounds; the percussion note over this area was slightly impaired; the lung gradually cleared. The note on this patient would hold good for all, save that in two the affection was of the right side and the heart was displaced over into the right chest. The same urgency and cyanosis, the same variation in the physical signs were apparent in all. The two cases of right-sided massive collapse are portrayed in Figs. 4, 5, 6, 7 and 8. Clearing in these cases was a matter of one to three weeks.

CASE IX.—Massive collapse of the unwounded side in a chest wound. Patient had been wounded four hours before, the bullet going through the right chest, fracturing one rib in its exit, he coughed blood at the time, had some dyspnoea and distress, but had begun to get over the shock of the wound. While being transported to the "Casualty Clearing," urgency in respiration began, and when seen he was seriously ill. It was apparent, however, that the bullet had gone in and out the right chest, that there was comparatively little sign of hemothorax, and that the left side had become quite solid, yet with good fremitus and

tubular sounds. An X-ray taken shortly after showed the absence of any signs of the heart to the right and the dense consolidation of the whole left chest. By next morning patient was much easier, no fluid was found in the solid chest and clearing was a matter of a few days.

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A very complete bibliography of post-operative pulmonary complications follows the articles by Scott, Jackson, Whipple; fat embolism was well described by Roswell Park in the *N.Y. Med. Journ.* (1884, Vol. xl), its surgical relations are well considered. Bissell (*Surg., Gyn. and Obst.*, 1917, Vol. xxiv) and Elting (*Ann. Surg.*, Sept., 1925) show the import of fat embolism in surgical cases.

THE LIFE HISTORY OF A CASE OF NEPHROSIS

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A PROTRACTED study of cases of nephritis extending throughout the life-cycle of the disease will clarify many phases of this difficult problem. Isolated observations over short periods fail to explain important points.

Friedrich Müller, several years ago, introduced the term "nephrosis" for a type of degenerative renal lesion. In 1914 Volhard and Fahr¹ extended our knowledge of the pathological changes taking place in the kidney. Their work aroused considerable discussion and criticism. Epstein,^{2,3} in 1917, published a more complete clinical description, championing the contention that it was a clinical entity. In a later publication Epstein⁴ has definitely stated that he believes nephrosis to be "a clinical entity"; that it is "essentially a metabolic disease," and is "characterized by changes in the protein and lipid content of the blood-serum." Furthermore, he states that the water retention and œdema are of extra-renal origin, being due to the reduced amount of blood-colloid which has caused a lowered osmotic pressure. Hence he thinks that a high protein diet is rational therapy. Other observers, notably Sir Clifford Allbutt,⁵ Box,⁶ McCay,⁷ Symes,⁸ and Rabinowitch,⁹ have reported cases, fulfilling in part at least Epstein's requirements, which improved with a high protein diet. Kahn,¹⁰ after an extensive study of cases of chronic parenchymatous nephritis, came to the conclusion that chronic nephrosis was a very rare condition. His report upon the unsatisfactory results obtained by feeding high protein diets is not conclusive since he was apparently unable to find a case that fulfilled Epstein's requirements. The unusual occurrence of this entity and its improvement under high protein therapy has also been critically discussed by Christian¹¹ and Geyelin.¹²

This is a report of a case of a young Chinaman who from the time of onset of his illness until death, thirty months later, was under close observation. During this period of 923 days, 451 of them, that

is, 46 per cent. of the duration of his illness, were spent in the hospital ward. After death an autopsy was obtained.

CASE REPORT

CASE No. 50.—Metabolism. T. C., male, aged eighteen.

Admitted to the hospital May 21, 1920, complaining of weakness and swelling of his legs, trunk, hands, and face.

Upon admission he was a typical case of nephrosis, the findings agreeing with those specified by Epstein. Unfortunately, data as to the blood-lipoids are missing. With the passing months the chemical findings could be well coördinated with the changes having taken place in the kidneys as shown at autopsy.

Present Illness.—The onset of the illness dated from the middle of April, 1920, when he was confined to bed for three days with what he described as a "fever." No data to indicate that he suffered from an infection could be obtained. Shortly afterwards his feet began to swell and he had to stop work. Gradually the swelling extended, involving his trunk, hands, arms, and face. There was no headache or backache. Weakness had been progressive.

Personal History.—Born in China, having come to Canada nine years previously. In China was confined to bed for two months with boils on the right side of his neck and on hands. No other illness recorded. Had never had a cough.

Family History.—Irrelevant.

Physical Examination upon Admission.—Weight, 69.54 kg. Height, 161.9 cm. Temperature, 98. Pulse, 70. Respiration, 20. The whole body was markedly œdematous with a protuberant abdomen. There was no dyspnœa. The mucous membranes were of fair color. The pupils were equal and reacted to light and accommodation. No evidence of past chronic disease was present. Teeth were in excellent condition and the throat was negative. The thyroid was not palpable and the lymphatic glands were not enlarged.

Respiratory System.—At both bases posteriorly there was a moderate amount of fluid, and throughout both lungs a few small moist râles could be heard.

Cardio-circulatory System.—Pulse slow and regular with soft vessel walls. Blood-pressure, 114/65. The heart was quite normal.

Gastro-intestinal System.—Abdomen bulging with evidence of marked ascites. No organs were palpable.

The other systems were negative except for marked œdema of both legs, and scrotum. All reflexes were normal.

The urine was scanty, highly pigmented, specific gravity of 1036 to 1042, albumin about 24 gm. per litre with a moderate quantity of globulin, and no sugar or acetone. The microscopic picture showed many hyaline and granular casts, some of which were covered with leukocytes undergoing fatty degeneration, a few renal cells, and many neutral fat-droplets. No red blood-cells could be found.

Blood.—Reds, 5,680,000; whites, 11,000; Hb, 95 per cent. (Palmer).

Stool.—Negative.

Fundi.—Normal.

Blood-chemistry.—Non-protein nitrogen, 35.0 mgm. per 100 c.c.; urea nitrogen, 18.2 mgm. per 100 c.c.; plasma chlorides, 5.8 gm. per litre; plasma proteins,

albumin, 1.40 per cent., globulin, 2.08 per cent. Total plasma nitrogen, 0.742 per cent.

Blood Wassermann.—May 26, 1920—++ (+)

July 6, 1920—Negative.

July 23, 1920—Negative.

The positive Wassermann reaction was considered to be due to the altered plasma proteins and increased blood-lipoid.

Unfortunately, at this time, no further chemical data were obtained, but the history, clinical and laboratory findings were sufficient to arouse the suspicion that there was a degenerative renal lesion of the tubular type, which closely resembled the picture of nephrosis as described by Epstein.

During the next year the boy remained continuously in the hospital. Subsequently he was re-admitted upon six occasions, while from May 4, 1922, until his death on November 29, 1922, he was in the ward almost constantly. The immediate cause of death was miliary tuberculosis, the complication developing in late October, 1922, resembling in its onset an attack of acute bronchitis. One week before death, tubercles were found in both choroids.

In Table I is recorded the general course of the case. The data are arranged in periods according to the diet given. Other values are approximated as near as possible to those actually found. Regardless of the fluctuations in oedema, contraction of the kidneys progressed with a urine of falling specific gravity. The blood showed a progressing secondary anæmia, while the blood-pressure remained low throughout. The fundi showed no vascular changes.

From admission until July 28, 1920, there was a progressive loss of oedema, the body-weight decreasing 50 per cent. (69 to 35 kg.). Corresponding changes took place in the urinary findings. Then without known cause the oedema began to return. On September 10, 1920, with a body-weight of 46 kg. a moderately high protein diet (P., 70; F., 14; CHO, 60) was started. At this time there was marked lipæmia. By October 15, 1920, the blood uræa nitrogen had risen from 16 to 61 mgm. per 100 c.c. and marked vomiting developed. The diet was stopped. Subsequently gradual improvement took place, but the oedema never completely disappeared. As the months passed, ability to concentrate became less and less, becoming fixed at a level of 1010 to 1012. Albuminuria of marked degree continued to the end, but casts became fewer and fewer. Coincidentally with inability to concentrate moderate nitrogen retention developed. Finally a terminal infection intervened, being the immediate cause of death. Throughout the whole course of the disease there was no evidence of involvement of the cardiovascular system.

CEDEMA AND PLASMA PROTEINS

Epstein has advanced the theory that the oedema of nephrosis is of extra-renal origin, depending upon the lowered osmotic pressure of blood due to the reduced amount of circulating colloid. Starling has shown that the osmotic pressure of the blood-proteins amounts to 25 to 30 mm. of Hg. Therefore with reduction of this intracapillary force there would be a relative increase in the osmotic pressure exerted by the intercellular fluids. To my knowledge Epstein has not

Nov. 15	42	50	57	234	0	800	1022	14	1.2	2,300,000	45	100	65	Fundi normal.
to	43													
Dec. 15	45													
Dec. 16	45	64	67	233	0	1500	1018	12	5.0	3,063,000	50	105	75	Improving.
to	46													
Jan. 3	1921													
Jan. 4	45	60	65	200	5	1600	1016	5	7.0	3,000,000	50	130	95	Edema almost gone.
to	46													
Feb. 17	39													
Feb. 18	39	70	80	250	5	1500	1018	8	7.0	2,800,000	58	125	90	Discharged, May 11, 1921.
to	40													
May 11	40													
July	40													
Aug.														
and	46													
Sept.														
1922														
May	60	45	70	105	0	2000	1012	++	...	3,280,000	50	100	70	Re-admitted, May 4, 1922.
to	61													
June	63													
July	55	45	70	95	0	1800	1012	++	...	2,750,000	40	100	60	Discharged, June 12, 1922.
Aug.	53	40	100	200	0	1600	1012	++	...	3,100,000	40	100	65	Only moderate cedema all winter.
Sept.	58	30	100	240	0	1500	1012	++	...	3,200,000	45	115	70	Re-admitted, July 6, 1922.
Oct.	59	30	100	250	0	1600	1010	++	...	1,390,000	30	120	80	Edema about stationary.
Nov.	50	40			0	1300	1012	++	...	1,810,000	35	110	70	Fundi normal.
Nov. 29	Died.													Acute bronchitis. Taking about 1200 cal. per day up until three days before death.

published any data proving this theory, nor have others presented observations disproving it. Upon it in part is based his treatment, namely, the high protein diet, which attempts to restore the lowered blood-colloids, thus raising the decreased osmotic pressure.

In Table II are presented data to show that upon admission there was a marked decrease in the total proteins with a reversal of the normal albumin-globulin ratio, this finding being typical of nephrosis (Epstein). By July 29, 1920, 34.5 kg. of œdema fluid had left the tissues while the globulin percentage of the total plasma proteins remained practically the same (55 per cent.). With this change the total plasma proteins had increased from 3.48 to 6.18 per cent., but this high level of plasma protein was of very short duration, dropping to 4.47 per cent. on August 11, 1920, with only a return of four kilograms of œdema fluid. Subsequently on February 22, 1921, again with very slight œdema, weight 39.3 kg., the total plasma proteins were 3.85 per cent. This would disprove Epstein's theory of the cause of the œdema in nephrosis.

As the renal lesion progressed there was a marked tendency for the normal albumin-globulin ratio to re-assert itself, this being more marked after January, 1921. The total plasma proteins remained below normal with the exception of the finding on May 5, 1922, when, after a fairly comfortable winter and spring, the œdema started to return. It is interesting to note that with this gain in œdema, the globulin percentage of the total protein remained at 39 per cent., the level which it had apparently held for the past year (May 3, 1921, to May 5, 1922). With the terminal acute infection the excessive œdema rapidly disappeared and the total plasma proteins, as well as its globulin percentage, fell.

Coördination of the plasma chlorides with the œdema shows that at times when the latter was greatest the chlorides were low. With elimination there was a marked tendency for them to rise, and as it returned the chlorides fell.

KIDNEY FUNCTION AND NITROGEN RETENTION

At the onset the urine volume was small with a high concentration. In ten months' time a marked inability to concentrate appeared (Table I), which progressed slowly, becoming fixed at a terminal

TABLE II
Edema and Plasma Proteins

Date	Weight	Plasma Proteins			Globulin Percent- age of Total Protein	Plasma Chlorides (as NaCl)	Remarks
		Albumin	Globulin	Total			
1920	kg.	%	%	%		gm. per l.	
May 20..	69.54	1.40	2.08	3.48	59.7	5.80	Admission.
May 31..	67.49	1.46	2.26	3.72	60.8	6.05	Extreme
June 15..	63.18	1.70	2.01	3.71	54.1	5.65	anasarca.
June 25..	61.47	1.71	3.30	5.01	65.8	6.50	Edema.
July 5 ..	51.81	2.30	3.01	5.31	56.6	7.05	Disappearing.
July 12..	51.12	1.36	3.24	4.60	70.4	6.55	
July 20..	41.81	2.56	2.60	5.16	50.4	6.55	
July 27..	36.36	2.76	3.42	6.18	55.4	5.80	
July 29..	35.00	No edema.
Aug. 11..	39.09	1.69	2.78	4.47	62.0	5.85	
Aug. 16..	42.94	1.69	5.87	Gradually
Aug. 23..	42.94	1.30	3.61	4.91	73.5	6.00	developing edema.
Sept. 24..	47.72	1.88	2.24	4.12	54.4	5.90	
Oct. 1 ..	45.67	1.73	1.89	3.62	52.2	5.75	
Nov. 30..	42.50	1.88	1.32	3.20	41.2	6.50	
Dec. 21..	49.09	2.03	2.45	4.48	54.6	6.00	Edema at peak.
Dec. 28..	48.00	1.41	2.90	4.31	67.1	6.10	
1921							
Jan. 14..	44.32	2.27	2.05	4.32	47.4	5.85	
Jan. 25..	45.00	3.50	1.22	4.72	25.8	6.10	Eliminating edema.
Feb. 1 ..	42.50	3.22	1.41	4.63	30.5	6.29	
Feb. 8 ..	40.68	2.21	2.15	4.36	49.2	6.40	
Feb. 16..	40.00	2.54	1.93	4.47	43.1	7.35	
Feb. 22..	39.32	2.29	1.56	3.85	40.5	7.40	Practically no edema.
Mar. 1 ..	43.18	2.12	2.30	4.42	52.0	7.05	
Mar. 8 ..	43.18	2.54	1.85	4.39	42.1	7.30	
Mar. 15..	44.54	2.49	1.09	3.58	30.4	7.40	Developing edema.
Mar. 24..	45.23	3.11	1.25	4.36	28.8	7.30	
Mar. 31..	46.47	2.71	1.31	4.02	32.6	7.25	
Apr. 19..	48.63	2.19	1.57	3.76	41.8	7.09	
May 3 ..	47.50	2.58	1.66	4.24	39.2	6.90	
Sept. 1 ..	44.20	2.75	2.01	4.76	42.3	
1922							
May 5 ..	64.20	4.47	2.92	7.39	39.6	6.56	Maximum
July 10..	56.81	2.49	2.09	4.58	45.6	(9th) 4.90	edema.
July 31..	52.50	2.31	2.18	4.49	48.5	(17th) 6.22	
Sept. 8 ..	58.41	2.20	2.86	5.06	56.5	(Aug. 7th)	
Oct. 28..	46.00	3.06	1.05	4.11	25.5	Losing edema.
Nov. 29..	Died.						

level of 1010 to 1012. Table III records concentration tests during 1921 and 1922.

It is of interest that this impairment of concentration antedated persistent urea retention by about one year.

TABLE III
Nephritic Test Meals

Date	Urine		
	Volume Night Urine	Maximum Specific Gravity	Nitrogen Concentration at Night
1921	c.c.		%
Mar. 1.....	700	1018	0.53
July 13.....	1150	1016	0.57
Sept. 3.....	890	1018	0.38
1922			
Aug. 2.....	670	1016	0.49

Concentration Test

Time	Urine		
	Volume	Specific Gravity	
	c.c.		
8-11 A.M.....	92	1017	No fluid given. Dry mixed diet. Body-weight stationary at this period. Nitrogen: Mixed day = 0.54 per cent. Night = 0.57 per cent.
11-2 P.M.....	125	1016	
2-5 P.M.....	130	1017	
5-8 P.M.....	158	1018	August 8, 1922.
8-8 Night.....	310	1018	
Total.....	815		

From May, 1920, to May, 1922, the urine was typical of a tubular degenerative nephritis (Table IV). Albumin was abundant, varying inversely as the volume output. Granular and hyaline casts were very numerous, but no red cells were found. Even during the period of high protein intake, September 10 to October 15, 1920, when the blood urea nitrogen increased from 16 to 61 mgm. per 100 c.c., no red cells were found. However, by the summer of 1921, casts were very much fewer. In May and June, 1922, upon eleven occasions red blood-cells in small numbers were found in the urine. Associated with the appearance of the red cells a moderate urea and creatinin retention developed which persisted until death. This was not associated with a rise in the blood-pressure. During the remaining

TABLE IV
Renal Function

Date	Blood			Phthalein	Urine
	Urea Nitrogen	Uric Acid	Crea- tinin	Two Hours	Microscopic
1920	mgm. per 100 c.c.			%	
May 21..	18.2	20	Granular and hyaline casts+++.
May 27..	23.9	Renal cells. Leukocytes on casts showing fatty changes. Neutral fat-droplets.
June 14..	27.3	Serum globulin.
July 19..	11.2	Same.
Aug. 3 ..	17.2	Same.
Sept. 6 ..	16.8	Same.
Oct. 15..	61.6	(High protein diet, September 10 to October 15.)
Nov. 30..	17.5	Same.
Dec. 28..	26.6	Same.
1921					
Jan. 3 ..	20.5	5.8	1.6	Same.
Jan. 14..	28.0	2.1	2.1	Same.
Jan. 25..	21.7	3.0	2.1	Same.
Feb. 1	2.5	2.0	Same.
Feb. 8	2.2	1.8	Same.
Mar. 2	7	Same.
Mar. 8	9	Same.
Mar. 15..	10	Same.
April 13..	25.2	7.5	Same.
July 12..	18.2	14	Fewer casts. Leukocytes+.
1922					
May 5 ..	39.2	3.1	3.6	10	Same plus a few red blood-cells upon eleven examinations during May and June.
May 9 ..	42.0	
May 15..	32.2	2.4	3.5	9	
May 31..	44.8	6.0	4.0	
June 6 ..	39.2	6.0	4.0	
June 12..	44.3	5.8	3.7	
July 7 ...	47.6	7.7	5.1	5	A few hyaline and granular casts. A few leukocytes.
July 14..	46.2	7	
July 25..	40.6	7	Same.
Aug. 1 ...	41.3	6	Same.
Aug. 7 ..	52.5	4.4	5.0	Same.
Aug. 17..	63.7	3	Same.
Aug. 28..	69.3	8.3	6.6	Same.
Sept. 5 ..	62.3	Same.
Sept. 15..	51.8	8.9	5.5	Trace	Same.
Sept. 18..	63.0	7.9	5.4	Same.
Sept. 29..	54.9	6.2	5.5	Trace	Same.
Oct. 9 ..	50.4	7.3	5.1	Trace	Very few casts. Many leukocytes.
Oct. 25..	66.5	10.3	5.2	Trace	Same.
Nov. 8 ..	36.4	7.0	4.6	Trace	Same.
Nov. 20..	47.6	5.7	3.3	Same.
Nov. 27..	45.5	8.9	5.2	Same.
Nov. 29..	Died.				

months of life, July to November, 1922, no red cells were ever found, and casts became very infrequent. White cells increased noticeably.

With the exception of the period of high protein feeding, no persistent retention of nitrogen in the blood occurred until May, 1922, two years after the onset. This was coincident with the appearance of red blood-cells in the urine, and followed a period of rapidly increasing edema. No infection was noted. With the urea retention moderate uric acid and creatinin retention followed. Even two days before death the values were practically the same as during the preceding five months.

Judging renal function by phenolsulphonephthalein excretion, a marked impairment was noted as early as March, 1921. By August, 1922, it had fallen to 3 per cent. in two hours, and from September on only a trace passed the kidneys.

Acidosis played little part in the course of this case. Respiratory symptoms never developed. Upon June 1, 1920, the CO_2 capacity of the plasma was 57.5 volumes per cent., and on October 9, 1922, it was 36.1 volumes per cent. At that time the plasma bases were normal; sodium 365, potassium 21, and calcium 10.8 mgm. per 100 c.c.

RENAL GLYCOSURIA

On September 22, 1920, the thirteenth day of the high protein diet (P., 78; F., 14; CHO, 60), when a rise in the blood-urea was taking place, glycosuria (6.99 gm.) developed. From this time on until death it was almost constant, the twenty-four hour amount varying from two to eleven grams, and having no relation to the carbohydrate intake. At irregular intervals a day would pass without glycosuria, and during one period of two weeks it was present by day and not at night. During the last few months of life the glycosuria did not increase, disappearing during the last three days of life. The blood-sugar was always normal. Table V records the essential findings.

Glucose excretion curves on March 7, and September 6, 1921, showed a fairly constant excretion rate throughout the twenty-four hours. In Table VI is recorded that of March 7, 1921.

The cause of this glycosuria is interesting to speculate upon. We know that glycosuria of the renal type not infrequently develops in nephritis of the "chronic parenchymatous" type. The fact that it developed after the institution of the high protein diet (thirteenth

day) would indicate that the excretion of nitrogen end-products caused tubular fatigue. This is contrary to Cushny's theory of

TABLE V
Renal Glycosuria

Date	Blood-sugar		24-hour Urine Glucose	Remarks
	a. c.	p. c.		
1920	%	%	gm.	
Sept. 22.....	6.99	First appearance of glycosuria.
Sept. 24.....	0.142	7.20	
Sept. 26.....	0.129	8.20	
1921				
Jan. 5.....	0.091	0.100	8.97	
Jan. 14.....	0.098	8.05	
Jan. 26.....	0.099	11.59	
Feb. 9.....	0.088	0.136	6.73	
Mar. 3.....	0.090	0.101	7.86	
Aug. 29.....	0.072	0.083	1.80	After three days' fast. CHO, 20 gm. for two days.
Aug. 31.....	0.082	0.086	2.70	
Sept. 1.....	0.071	3.50	
Sept. 5.....	0.092	3.60	
1922				
Aug. 21.....	0.087	5.76	Two days before death.
Nov. 27.....	0.091	0	

renal secretion which assumes that the tubules absorb water only. Accepting this theory it is possible that the diuretic action of the

TABLE VI
Glucose Excretion Curve

Time	Urine		Glucose	
	Volume	Specific Gravity	Per Cent.	Total
	c.c.			gm.
8-10 A.M.....	116	1022	0.71	0.82
10-12 A.M.....	138	1020	0.63	0.87
12-2 P.M.....	152	1021	0.66	1.00
2-4 P.M.....	142	1022	0.69	0.98
4-6 P.M.....	170	1022	0.56	0.95
6-8 P.M.....	140	1021	0.67	0.94
Total day.....	858			5.56
Night 8-8.....	775	1019	0.55	4.26
Total.....	1633			9.82
Intake.....	1500			

urea resulted in a greater call on the part of the tubules to absorb water, thereby resulting in their fatigue.

BASAL METABOLISM

With the prolonged under-nutrition the patient's skin became very dry and in his later months definite ichthyosis developed. At no time was the thyroid gland palpable. The basal metabolism on August 5, 1922, was 29.6 per cent. below normal. (Weight, 53 kg.; surface area, 1.55 sq. m.). At this time there was moderate œdema.

POST-MORTEM, NO. 4211, NOVEMBER 30, 1922

External Examination.—The body is that of a young Chinaman, appearing to be of stated age. Nutrition is good and development is average. The skin is dry and inelastic and there are white striations over both flanks.

Thorax.—In each pleural cavity there is a cupful of clear serous fluid. The lungs are voluminous and free throughout. On opening the pericardium about 75 c.c. of clear serous fluid are present. The pericardial surfaces are smooth and glistening with no adhesions. The mediastinal glands are enlarged, anthracotic, and show irregular cheesy, necrotic areas. *Left Lung.*—Weight, 850 gm. The lung is congested but subcrepitant throughout. Its surface is covered with minute whitish tubercles which are especially marked in the interlobar fissures. The cut surface is densely studded with fine tubercles. *Right Lung.*—Weight, 980 gm. Findings are the same as in the left lung. *Heart.*—Weight, 200 gm. The heart is of normal size. The mitral valve is intact. The cusps of the aortic valve are intact, but immediately above the orifices of the valves and surrounding the orifices of the coronary arteries are well-marked fatty intimal thickenings. The endocardium of the ventricles is negative. The ventricular walls are thin and flabby, but the musculature is tough. The coronary arteries are patent.

Abdomen.—The subcutaneous fat is 1.8 cm. thick. The peritoneal cavity contains a large quantity of clear yellow fluid. The lower border of the liver is 5 cm. below the xiphoid cartilage in the midline. Isolated tubercles are present on the peritoneal surface of the small intestine. *Spleen.*—Weight, 420 gm. The capsule is smooth and tense. The pulp is very soft with prominent malpighian corpuscles and a few small pin-point sized tubercles. *Left Kidney.*—Weight, 60 gm. The kidney is of the usual shape with normal pelvis and ureter. Its vessels are small and not markedly arteriosclerotic. The capsule is a little opaque. The cut surface is a quite pale, grayish-yellow color. The cortex and medulla are poorly differentiated. In the cortex the vascular markings are lost. Upon stripping the capsule it is found to be only slightly adherent, leaving a finely granular surface which is studded with fine pin-point sized tubercles. The peripelvic fat is increased. *Right Kidney.*—Weight, 55 gm. The findings are the same as in the left kidney. *The bladder* shows tubercles about the trigone. The *bone-marrow* is of a pale yellow color and very fatty. The *stomach* and *intestinal tract* are negative. The *liver* weighs 1370 gm., has a thin, smooth capsule and in the right lobe there are a few tubercles. The *pancreas* and *brain* are negative.

Anatomical Diagnosis.—(1) Productive nephritis (small white kidneys). (2) Miliary tuberculosis of the lungs, spleen, liver, adrenals, peritoneum, and bladder. (3) Tuberculosis of the mediastinal glands. (4) Early fatty changes in aorta. (5) Ichthyosis. (6) Hydrothorax. (7) Ascites.

Histological Examinations.—Kidneys.—The sections show a very widespread productive lesion. The changes in the glomeruli are marked, showing all stages of thickening of the capsule, fibrosis, and atrophy of the tufts to complete hyaline destruction. There is a generalized increase of the connective tissue between the tubules which, however, is more marked in certain areas producing a slight island appearance. Many of the tubules contain casts, hyaline, granular, or cellular. The epithelium lining the tubules shows varying stages of granular disintegration. Also there are scattered tubercles consisting of the typical epithelioid proliferation with slight or early central necrosis, and a very marked peripheral round-celled infiltration. *Lungs.*—Throughout both lungs the normal tissue is replaced by typical small tubercles. *Other Organs.*—The *spleen* is studded with small tubercles while the *pancreas* shows a very few. In the cortex of the *adrenal* a few are found. The normal tissue of the *mediastinal glands* is replaced by tuberculous inflammatory tissue with central areas which have undergone caseation and coagulation necrosis. The *liver* shows many tubercles.

DISCUSSION

This case, answering in all details at the onset of the illness the requirements of Epstein's nephrosis, died with small white kidneys, which showed marked productive changes. The picture of the progress of the lesion as shown from the clinical and chemical data is fairly complete. The patient did not die of renal failure but of an intercurrent infection. The autopsy findings showed the stage to which the renal lesion had advanced.

That this case was one of nephrosis at the onset is supported by the following findings: (1) The patient was a young person. (2) The onset of the illness was obscure. (3) Œdema was extreme with hydrothorax and ascites. (4) The urine was quite characteristic. (5) The blood showed the typical protein alterations. (6) There was no non-protein nitrogen retention. (7) Secondary anæmia was progressive and there was no change in the cardiovascular system. Blood-pressure remained normal. (8) The blood-cholesterol was undoubtedly increased for there was visible lipæmia. (9) The heat production was decreased.

Epstein's theory that the cause of the œdema is due to the lowered blood-colloids in this case is not substantiated. Table II shows that the œdema was fairly independent of the total plasma protein; and that the albumin-globulin ratio had little relation to the degree of œdema. The institution of a high protein diet was not followed by improvement, but resulted in non-protein nitrogen retention, which disappeared shortly after discontinuing the diet. The fact that the

appearance of red blood-cells in the urine coincides with the persistent rise in the blood non-protein nitrogen bodies, would possibly indicate that after two years of a degenerative renal lesion the glomeruli had become involved. From this time on the lesion was of a diffuse productive nature, shortly marked changes in the ability to concentrate appearing. However, with glomerular involvement there was no cardiovascular change. The occurrence of persistent glycosuria is of great interest as it is usually associated with tubular involvement. That the high protein diet seems to have a relation to its onset is of significance, and that during the first few weeks of its appearance it was usually present by day and not at night might indicate that the excretion of nitrogen end-products bore a causal relationship. The low metabolism I consider to be of the nature of a secondary hypothyroidism. The thyroid gland is not anatomically defective, but due to the prolonged state of under-nutrition the "tissue call" for thyroxin fails. A similar state was frequently seen in diabetes mellitus, before the advent of insulin. With restoration of general nutrition, heat production returned to the normal level. The fact that the autopsy findings showed no evidence of syphilis would substantiate the idea that the positive blood Wassermanns were due to the altered blood-colloids.

CONCLUSIONS

It would appear that the clinical condition termed "nephrosis" is a progressive disease, and that if the case escapes a terminal secondary infection for a long enough time, the primary renal state will progress into a contracted kidney.

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Surgery

A DAY IN DR. CHARLES H. MAYO'S CLINIC

- | | |
|--------------------------------|--|
| (1) Avian Tuberculosis. | (5) Cholecystitis. |
| (2) Simple Ovarian Cysts. | (6) Stricture of the Common Bile-duct. |
| (3) Fibromyomas of the Uterus. | (7) Duodenal Ulcer. |
| (4) Exstrophy of the Bladder. | |

By WILLIAM A. HENDRICKS, M.D.

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THE following cases, in which operation was performed by Dr. Charles H. Mayo August 28, 1925, are reported because of their individual interest and the diversity of the diseases treated.

REPORT OF CASES

CASE I. *Avian Tuberculosis*.—A woman, aged twenty-two, came to the clinic August 18, 1925, because of pains beneath the lower end of the sternum, radiating through to the back, and a mass in the abdomen which had appeared three months previously. The pains came on suddenly, lasted for from one to two hours, then disappeared suddenly. There was no tenderness, nausea, vomiting, or dyspepsia. The spells of pain always followed eating fried food.

Examination revealed a large tumor of the left upper quadrant of the abdomen, extending to the median line and to the umbilicus. The tumor was definitely notched, firm and smooth, but not tender. The systolic blood-pressure was 130, the diastolic 75, the pulse-rate 120, and temperature 98.6°. The patient's weight was normal (147 pounds). The examination of the urine was negative. The hemoglobin was 72 and 61 per cent. Erythrocytes numbered 4,780,000, leukocytes 5000, the differential leukocyte count showed 19 per cent. lymphocytes, 2 per cent. large mononuclears, 4 per cent. transitional cells, 74 per cent. neutrophiles, and 1 per cent. eosinophiles; the platelets numbered 98,000. The coagulation time was six minutes, bleeding time one minute. The Wassermann reaction was negative. The calcium coagulation time was seven minutes. The fragility was normal. Viscosity was 1:4.2, the acid hematin 78 per cent., hematinoidin 36 per cent., total blood volume 78 c.c. for each kilogram of body-weight. Röntgenograms of the chest showed some bronchial thickening. A diagnosis was made of splenomegaly, indeterminate in type.

At exploration the spleen was found to be lobulated, about 27.5 cm. long, 15 cm. wide, and 7.5 cm. thick. There were several accessory spleens, one measuring 7 cm. and another 2 cm. The liver was studded with small yellow, smooth areas. At the juncture of the common duct was a large gland measuring about 1.5 cm. in diameter. The spleen and two small accessory spleens were removed.

A pathologic diagnosis was made of tuberculosis of the spleen and tuberculosis of the liver and mesenteric glands of the avian type.

Comment.—This is the second case of avian tuberculosis of this type that has come to the attention of Dr. C. H. Mayo. In this case the spleen, liver and some of the mesenteric glands were affected. There were no marked blood changes nor fever, nor was there any appreciable physical disability. The patient convalesced uneventfully and was dismissed from the clinic the twentieth day after operation.

Von Kurt Lederer reported a case in which avian tuberculosis was associated with polycythæmia. There were almost 10,000,000 erythrocytes and the hemoglobin was 140 per cent. (Sahli). At necropsy the spleen, kidney and lungs showed tuberculous lesions, but the organs were not overfilled with blood and there was no hyperplasia of the marrow of the long bones. His case was similar to the early cases of polycythæmia with primary tuberculosis of the spleen cited in the French literature; the bacilli in his case, however, were of the avian type.

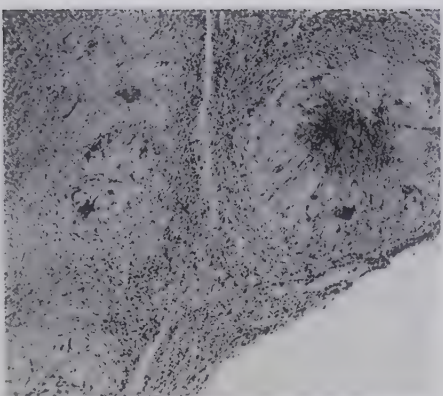
Loewenstein believes that this kind of tuberculosis may be carried by the food and enter the circulation through the intestine. Enlargement of the spleen is almost always present and the bone-marrow and kidney are points of predilection. He had found both erythæmia and leukæmia in association. Several other cases of avian tuberculosis in man have been reported.

Lipschutz described the lesions as containing some of the usual elements of tuberculous tissue, but polymorphonuclear cells were more frequently found than lymphocytes. Caseation was completely lacking. (Figs. 1, 2, 3 and 4.)

Jousset found that the avian bacillus had a very moderate degree of local caseating power and that the tuberculin extracted from these bacilli had no local or general specific immunizing effect on the tuberculous animal whether affected by human or bovine bacilli. Jousset states emphatically that the avian bacilli must not be identified with the human and bovine types.

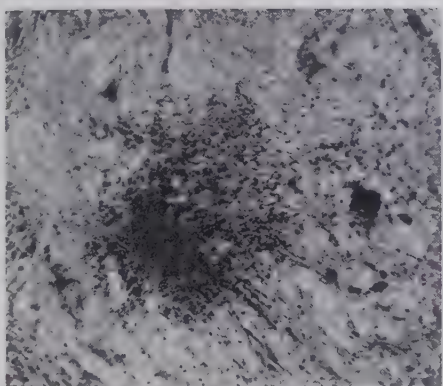
CASE II. Simple Ovarian Cysts.—A woman, aged thirty-one, registered at the clinic August 18, 1925. She had complained of abdominal pain for eight months. In December, 1924, she had had an attack of severe pain lasting about two days, without nausea or vomiting. This pain was described as being over the entire area of the abdomen. At the same time she had had low abdominal crampy pains during the menstrual period, associated with pain in the lower right abdomen. In February, 1925, she had a second attack of generalized abdo-

Fig. 1.



Avian tuberculosis of the spleen in man showing tubercles with a few foreign-body giant-cells, numerous large epithelioid cells and waxy substance in the centre.

Fig. 2.



High magnification of one of the tubercles shown in Fig. 1.

Fig. 3.



Condromate tubercle in the liver of a fowl showing numerous large epithelioid cells.

FIG. 4.



The external surface of the spleen presented numerous nodules varying from 1 mm. to 2 cm. in diameter. These nodules (conglomerate tubercles) bear a close resemblance to the cortical abscesses of acute purulent nephritis. On section the nodules or tubercles stand out in relief giving the surface a "pebble-dash" effect. Foreign-body giant-cells are present in some areas. A number of the tubercles contain a waxy substance instead of the caseous material that is often found in the tubercles in cases of tuberculosis in man. In many tubercles there is no caseation, the centre being composed of large epithelioid cells in great numbers, which give a characteristic appearance to the avian lesion, in contrast to human and bovine tuberculosis. Lymphocytes are relatively less numerous than in the lesions in man.

minal pain again without vomiting, and this time a diagnosis of appendicitis was made. In April, 1925, she had a most severe attack of pain in the abdomen, associated with vomiting. At this time a diagnosis of intestinal intoxication was made. During the last attack she had much residual soreness in the lower middle and right zones of the abdomen. Two of these attacks were associated with the menstrual period, although ordinarily there was no pain at this time.

The patient weighed 123 pounds, and was 5 feet, 9.5 inches tall. Temperature and blood-pressure were normal. The lower abdomen was tender, more on the left than on the right side. Pelvic examination was difficult, but there was some thickening and tenderness in both adnexa. Blood-count was normal; urine, normal, and the Wassermann test negative. Röntgenograms of the teeth showed peripheral infection 2. The tonsils were enlarged, 2, and there were some deeply buried plugs in the tonsillar tissue. Röntgenologic examinations of the chest and colon were negative.

The pre-operative diagnosis was chronic appendicitis. Because of the history of abdominal pain, at times associated with the menstrual period, together with some soreness and tenderness in the adnexa, it was thought that exploration was warranted and a low median-line incision was chosen to explore appendix and pelvis.

The appendix showed chronic inflammation with obliteration at its juncture with the cæcum. It was about 4 cm. long with bulbous tip. There was a tumor of the left ovary about 10 cm. in diameter which was quite adherent, but the adhesions were easily separated. There was a cyst of the right ovary 6 cm. in diameter. The cysts of both ovaries were ruptured. The left ovary was excised and part of the left tube resected, and in the case of the right ovary, part of the hilum and a considerable part of the ovarian shell were preserved for menstrual function. On account of the irritation of the fluid two quarts of warm water were used to irrigate the operative field which was then dried by aspiration. The appendix was amputated.

The pathologic report was simple hemorrhagic cyst of the left ovary (ruptured); chronic salpingitis; small cyst of the right ovary; and chronic catarrhal appendicitis.

Comment.—The patient had taught school for thirteen years, and when admitted manifested some of the characteristics of nervous exhaustion. She was slightly irritable, restless, somewhat impatient, and gave a history of tiring easily. She had consulted several physicians who had diagnosed her disease as appendicitis and ptosis of the colon, and advised that she required operative treatment and a rest from her work. The abdominal pain and residual soreness resembled that of chronic appendicitis.

It frequently happens that in a patient of this type the diagnosis of nervous exhaustion is considered complete in itself, and a complete, satisfactory and thorough examination is consequently not made. It is sometimes recommended that the patient is in need of a

change and rest from her work, and she goes from one physician to another without getting relief.

Exploration revealed not only a chronic condition of the appendix but also cysts of both ovaries which seemed sufficient to cause insult and irritation to the nervous system and to give rise to the state of exhaustion and nervousness. In the removal of these cysts it was borne in mind that the patient was still in the menstrual age and that the ovarian tissue should be saved if possible, because of the frequent association of nervous symptoms with total removal of the ovarian tissue. Consequently, as much of the right ovary as possible was spared for menstrual function. Both cysts were simple with hemorrhage into the left one.

The etiology of glandular cysts depends on the structure from which they originate, and four theories deserve special consideration: (1) That they spring from the granulosa cells of the graafian follicle; (2) that downgrowths of the germinal epithelium from the surface of the young ovary become snared in the stroma of the ovary and later in life develop into glandular cystomas; (3) that pseudomucinous cystadenomas are in reality teratomas in which the characteristic glandular structures overwhelmingly prevail and that the serous cystadenomas arise from the germinal epithelium and from isolated downgrowths of the same, or from the follicular epithelium, and (4) the theory which seems most likely, that glandular cysts of the ovary arise from embryologic remains of the wolffian tubules. The contents of the cysts vary according to the type of epithelium lining the cystic spaces and glands, and according to the accidents which have occurred during the life of the tumor. The glandular epithelium in most glandular cystomas is of the high columnar goblet type and secretes a thick, glairy, semi-opaque, tenacious fluid.

Although ovarian tumors are most common in patients of the age of the menopause or later, they are occasionally encountered in children about the age of puberty.

Although there was a history of well-defined appendicitis, it was considered advisable to make a low incision in the median line in order to explore the pelvic organs. McBurney's incision, except in children or in cases in which there are definitely no complications, is not as frequently used as it was in the early days of appendiceal surgery. An incision through the right rectus near the median line

allows much more freedom for exploration in cases in which disease is suspected in more than one organ. Convalescence was uneventful.

CASE III. *Fibromyomas of the Uterus*.—A woman, aged fifty-two, registered at the clinic August 25, 1925, complaining of irregular menstruation. Previous operations, cholecystectomy and appendectomy, were performed here in 1923. Menstruation was normal up to and including April, 1925, but was absent in May. Discharge was very meagre on the menstrual day in June (about the first of the month). June 17, menstruation began unexpectedly and continued until the time of examination. July 23, curettage was performed but malignant disease was not found.

The pulse was 70, the temperature 98°, the systolic blood-pressure 128, and the diastolic 74. Examination of the abdomen was negative and the urine was normal. Hemoglobin was 70 per cent., the erythrocytes numbered 4,150,000, and the leukocytes 7000. The Wassermann reaction was negative.

The cervix was large, soft and patulous, and there were small nodules within the cervical canal. The uterus was retroflexed and irregular, and contained small fibromyomas.

At operation a large cystic wide-open cervix was found. There were purulent cystic pockets scattered throughout the uterus which was retroflexed above and below the internal os. The uterus was turned forward and vaginal hysterectomy performed, a clamp being placed on the broad ligament on each side and packed around with gauze, one strip of gauze being caught in the clamp. Since malignant disease was not found in the uterus the tubes and ovaries were preserved. After the uterine body had been cut free and removed, the clamps were left in position for seventy-two hours. They were loosened and unlocked four hours before being removed. The gauze pack was left three days longer. Since a degenerating uterus is likely to become a focus of infection with unnatural discharge from it between periods, hysterectomy is indicated, by the safest possible method for the case in hand.

Comment.—In a patient at the age of fifty-two with irregular bleeding or extensive flow, it is always wise to consider the possibility of malignant disease; until it has been proved to be benign, procedures should be instituted to define the cause of the bleeding. In this case, in spite of the previous dilatation and curettage, the bleeding had persisted and because of the patient's age and symptoms and the soft cervix and fibromyomas of the uterus it was thought best to remove the uterus. The vaginal hysterectomy was chosen because the size of the pelvic outlet would permit of convenient and quick extirpation of the organ. The uterus was found on microscopic examination to contain multiple fibromyomas; the endometrium was polypoid, and marked cystic cervicitis was present. It is this type of cervicitis together with disease of the teeth and tonsils, and the prostate gland in men, which constitutes the focus of infection in cases

of arthritis. The cervix plays a prominent part in the arthritis of the small joints of the hands and feet. The fibromyomas also are undoubtedly the result of the toxic stimulation of uterine muscle in local areas. Fibromyomas are present in a considerable percentage of cases in which menstruation continues after the age of fifty, the irritation and extra blood supply incident to the tumors prolonging the menstruation.

CASE IV. *Exstrophy of the Bladder.*—A boy, aged twelve, came to the clinic August 4, 1925, because of exstrophy of the bladder. He was about ten pounds under-weight. There was exstrophy of the bladder with failure of formation of the pelvis in front, and a tendency to bilateral inguinal hernia. Otherwise nothing abnormal was discovered.

The first stage in the operative treatment had been carried out August 7, 1925, when the right ureter was transplanted into the rectosigmoid (Coffey). Through a right lower abdominal incision, the ureter was isolated and divided close to the bladder. For the transplantation of the ureter into the rectosigmoid, catgut alone was used for suture. The exposed ureter was covered by attaching the sigmoid to the peritoneum posteriorly. The second stage had been carried out August 17, 1925, chromic catgut having been used. The left ureter was transplanted into the sigmoid. There was a slight amount of free straw-colored fluid in the peritoneum.

The patient was now appearing for the third stage of the operation. It consisted of excision of the bladder and distal ends of the stumps of the ureters and closure of the skin.

After the first operation, the transplantation of the right ureter, the patient did not void urine through the rectum for about four and a half days. This was tested out frequently by a rectal tube. During this time the temperature varied from 101° to 102°, and the pulse-rate was 120. Subsequent to the transplantation of the left ureter, from 750 to 1000 c.c. of urine were obtained by rectal tube.

Comment.—Exstrophy of the bladder occurs in about one of 50,000 persons and is associated with other developmental defects, such as lack of union of the symphysis. Frequently spina fibida occulta is found and in most cases there is bilateral hernia as well as absence of the umbilicus. These children should not be operated on earlier than the age of four or five years, because they have not learned to control the rectal content and manage their clothing at stool.

In all of the operations performed, the right ureter has been transplanted first into the sigmoid so that the operation may be facilitated by the loose bowel, which has to be transposed to the right side. The left ureter is transplanted secondarily from seven to fourteen

days after the first operation, depending on the patient's convalescence, and the bladder mucosa and stumps of the ureters are usually excised from seven to ten days after the second operation. The ureter is exposed transperitoneally and cut off as close to the bladder as possible; the distal stump of the ureter is ligated and the proximal stump dissected back from 3.5 to 5 cm. The bowel is fixed in clamps and the serosa and muscularis are cut through to the mucosa. A ligature or suture is applied to the open end of the ureter and the short end of the catgut is threaded into the lumen 8 cm. to insure its remaining patent. The ureter is then guided through the incision in the mucosa directly into the bowel and is anchored inside of the bowel about 2 cm. below the incision in the mucosa. The muscularis and serosa are sewed over the ureter, which lies in a very narrow trough, a distance of about 3.5 cm. The knot which anchors the ureter into the bowel is oversewed because it is contaminated in passing from the interior of the bowel. This operation of guiding the ureter underneath the serosa and muscularis into the bowel was introduced by Coffey. The bowel is anchored to the parietal peritoneum so that there may not be swaying and tension on the ureter. When the ureter is very much dilated it is often dangerous to transplant for fear of pyelonephrosis. The left ureter is transplanted into the bowel in the same manner.

Invariably after the first operation there is a temporary diminution of urine and rarely a temporary suppression. The rectal tube will disclose no urine from the rectum for four or five days, although sometimes within from twelve to twenty-four hours there may be urine present. The first transplantation is usually associated with some pyrexia and rise of pulse. The transplantation of the left ureter is invariably free from any untoward complication. Since the catgut has been inserted up the ureteral lumen there has been no trouble from urinary obstruction, even temporarily.

Following operation the patient comes to a stage where he can control the output of urine through the rectum very conveniently, and he is forever free from the annoying drainage of urine into his clothing. There have been three cases in the clinic in adults in which, transplantation not having been carried out, the mucosa of the bladder has been exposed to the irritation of clothing for many years and carcinoma has developed. In these cases the ureter has

been transplanted into the abdominal wall and the mucosa of the bladder removed. If ten days are allowed to elapse between transplantations the colon develops urinary tolerance, and absorption of urine ceases. There are no serious symptoms of fever with the second transplantation. This is probably simpler than the double ureteral catheters inserted into the ureters extending into the lumen of bowel and out of the anus.

CASE V. Cholecystitis.—A woman, aged forty-two, came to the clinic July 23, 1925, because she had been told she had fibromyomas of the uterus. Appendectomy had been performed previously. The left ovary had been removed during laparotomy for post-traumatic abdominal conditions. Laparotomy was again performed three years later, for acute obstruction. Following operation for post-operative hernia the convalescence was stormy, being complicated by pneumonia and the development of a perirectal abscess. She now complained of abdominal pain and poor general health. When palpated the abdomen seemed unduly firm in both lower quadrants. On pelvic examination, although the uterus was in good position, masses could be felt, which on bimanual pressure moved with the uterus. Dr. C. H. Mayo was of the opinion that there was a tumor involving the left side of the fundus, and advised exploration and probably hysterectomy.

Subtotal abdominal hysterectomy was performed for myomas of the uterus July 27th. At the time of this operation the gall-bladder was palpable from below, but no stones could be felt. Convalescence was satisfactory until about three and a half weeks after operation, when there was an attack of pain in the right upper abdomen with vomiting and rigidity.

Operative treatment was now being instituted for cholecystic disease. Exploration revealed a congested liver to which the gall-bladder was adherent. The lymph-nodes along the ducts were enlarged. The gall-bladder was very tense and filled with thick tarry bile and was of the "strawberry" type. Cholecystectomy was performed. The gall-bladder was adherent to the colon.

Comment.—A diseased gall-bladder can often reflexly cause spasm of the pylorus, and produce gastric symptoms with retention. It has often been noted that a low acidity or no free hydrochloric acid is present with chronic disease of the gall-bladder. Normally the edge of the liver is sharp and well defined and is often referred to as being axe-like. In diseases of the gall-bladder the part of the liver immediately surrounding this organ becomes cirrhotic. The content of bile salts is normally ten times as great in the bile of the gall-bladder as it is in that of the hepatic ducts. In a diseased gall-bladder, as in this one in which the bile was very thick and tarry, the amount of bile salts in the bile of the gall-bladder was probably twenty times as great as in the bile of the hepatic ducts.

CASE VI. Stricture of the Common Bile-duct.—A woman, aged forty-four, registered at the clinic August 18, 1925, complaining of gastric pain and jaundice. Her first illness began in April, 1924, when she had typical gall-stone colic with fever and slight chills. Morphine was given for relief. Jaundice lasted from seven to ten days and then gradually disappeared. The next attack came in the autumn of the same year, and the last in December; neither was associated with chills and fever. The gall-bladder had been excised in January, 1925. The patient was quite well for six months after operation. In June, there was an attack similar to the first one, but not so severe, and accompanied by slight fever with chills. Jaundice with itching of the skin was again present. The last attack occurred eight days before admission, the pains being of the typical colicky type and extending through to the back.

The patient was jaundiced (grade 2), and the sclerotics were tinged (grade 3). She had lost seven pounds in six months. The systolic blood-pressure was 120, the diastolic 80, the pulse-rate 80, and the temperature 98.4°. The urine contained bile. The hemoglobin was 70 per cent., the erythrocytes numbered 4,470,000, and the leukocytes 8500. The Wassermann test was negative. The coagulation time was twelve minutes, and the calcium coagulation time was ten minutes. The serum bilirubin was 12.2 mg. for each 100 c.c. The diagnosis was stone or stricture of the common duct.

The common duct was located near the point where the cystic duct had been removed. With a hypodermic needle the hepatic duct was easily found and opened and the stricture in the common duct located. The stricture was easily dilated and opened and a Mayo-Sullivan tube passed into the common and hepatic ducts, with a ring into the hepatic duct from the common duct. The Mayo-Sullivan tube is the bell end of a catheter over which two or three rings of rubber catheter two sizes larger are pulled to act as shoulder pieces; the bell end of the anastomosing catheter with its shoulder is pushed up into the hepatic or common duct and the smaller end with its shoulder is inserted into the lumen of the duodenum so that the catheter can neither drop down in the duodenum nor recede upward into the common duct. If the tube should remain longer than several years and become so coated with bile salts as to cause obstruction it may become necessary to remove it. In one such case removal of the tube was necessary.

Comment.—This case is interesting in that the patient's previous operation was in some measure the reason for her coming here. Cholecystectomy had been performed, and in the ligation of the cystic duct no doubt the common duct had been injured. The symptoms did not return until about six months after operation. The patient did not know whether stones were present or not at the time of removal of the gall-bladder. A test of hepatic function was made here and the serum bilirubin was found to be 12.2 mg. for each 100 c.c. of blood.

The two outstanding dangers in operation on the gall-bladder are damage to the common duct when an overlying gall-bladder is adherent to the duodenum and cystic and common ducts, and slipping of

the ligature after the cystic artery has been ligated. In the latter case one must be very cautious in reapplying the clamps, as here again the danger of injuring the common duct is very great.

It is often difficult to locate the ducts when scar tissue is present. The stricture may include a very short portion of the duct, or it may extend over a distance of 2 cm. A very good guide to the location of the ducts is a hypodermic syringe and needle. In this way the presence of blood or of bile in the constricted tissues can always be determined.

The type of anastomosis applied in this case was that in which the Mayo-Sullivan tube is used. This is the original Sullivan device modified by Dr. C. H. Mayo by the addition of two rubber rings slipped over the three-inch catheter. The bell or larger end of the catheter was guided into the hepatic duct and the small end of the catheter into the common duct below and thence into the duodenum. In some instances it is necessary to make an anastomosis between the proximal portion of the common duct and the duodenum when the distal portion of the common duct is constricted. In one instance the tube came away in six weeks and another stricture was the result. The rubber tube remains in place usually for months and has been found there three years after the original operation. The patient's convalescence was uneventful and the jaundice began to abate very appreciably during the first week; in two weeks it had almost disappeared.

In this instance the anastomosis was made between the hepatic and common ducts, the stricture of the common duct being bridged because there was sufficient common duct left for an anastomosis.

CASE VII. Duodenal Ulcer.—A man, aged sixty-one, registered at the clinic August 18, 1925, complaining of flatulence and loss of weight. For twenty years he had had an attack of stomach trouble once in five weeks, manifested by bloating, flatulence and a burning sensation in the stomach. The more recent attacks had been coming on about midnight and were relieved by soda. He sometimes vomited and was usually constipated. He had intolerance for boiled cabbage, pickles, and tomatoes. The day before admission he had an attack at midnight with vomiting. He had had la grippe twice. He had lost twenty-five pounds in four months.

The clinical examination revealed no abnormality except tonsillitis, grade 2. The total gastric acidity was 76, and the free hydrochloric acid 60. The blood-urea was 27 mg. for each 100 c.c. Röntgenologic examination of the stomach showed a lesion at the outlet with retention. The diagnosis was ulcer of the outlet of the stomach with retention.

At operation a duodenal ulcer was found in the first portion of the duodenum just below the pylorus. The duodenum was adherent to the liver, and the gall-bladder to the duodenum. The liver showed marked congestion, was thickened with rounded edges, and was cirrhotic near the gall-bladder. The gall-bladder was inflamed and the lymph-nodes were swollen. The appendix was chronically inflamed, grade 2. Posterior gastro-enterostomy and appendectomy were performed.

Comment.—Physical examination did not reveal any palpable mass in the abdomen nor any glandular involvement in the supra-clavicular region. The röntgenogram showed a lesion at the outlet of the stomach with retention. The history, the physical findings and the laboratory tests led one to consider the lesion benign. The duodenum is very infrequently the seat of a malignant process but gross lesions of the stomach are very prone to be malignant. It is particularly with this in mind that the surgeon resorts to gastro-enterostomy for duodenal lesions and it is because of this also that in case the lesion is gastric, particularly when the tumor is more than 2.5 cm. in diameter, it may be advisable to resect the stomach.

The area of the upper right rectus is chosen for the incision in cases of gastric or cholecystic disease. Through this incision the appendix and the pelvis can be examined. In this case not only was the lesion at the outlet of the stomach found as depicted by the röntgenogram, but extensive adhesions were discovered around the pylorus and gall-bladder where the duodenum had perforated. The gall-bladder showed chronic cholecystitis with swollen glands. The liver was markedly congested with some cirrhosis near the gall-bladder, which is a very common finding in association with gall-bladder disease. The acids in this case showed a total of 76, while the free hydrochloric acid was 60. It is expected that they will fall from 20 to 30 points after gastro-enterostomy. It is interesting to note that, if this decrease in acidity does not occur after operation, and if such foci of infection as infected tonsils or diseased teeth or appendix or inflamed gall-bladder are not eradicated, it is very possible that the ulcer will recur. In some cases the duodenal ulcer recurs and in others a gastrojejunal ulcer forms. This patient is to be advised about continuing his post-operative diet for a period of from two and a half to three months; he is to smoke very moderately if he wishes, but he ought to refrain from smoking entirely, and he is to abstain from alcohol. All foci of infection are to be eradicated. It is sometimes well to advise the patient to continue taking alkalis

for from six to ten weeks after operation. When the acidity is moderately high it should be controlled while the ulcer is healing. It has been noted that when the patient remains free from symptoms for a year or two after operation, the danger of recurrence is less, although there is sometimes recurrence ten or twelve years after operation.

In this case the gall-bladder is to be removed when the patient has recovered sufficiently from this operation.

Dr. C. H. Mayo does not believe that in cases of ulcer of the duodenum resection of the stomach is required to diminish the acids when there is no lesion of the stomach. Resection of the stomach may be seriously considered in cases of gastric lesions, particularly in cases of large ulcers which are prone to become malignant.

DIAGNOSIS AND TREATMENT OF ACUTE SUPERFICIAL CIRCUMSCRIBED ABSCESS

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ACUTE circumscribed abscess is one of the most common conditions requiring surgical treatment and it is important that its severer complications be well recognized and its treatment well standardized. The treatment of abscess is not so simple that it should be undertaken without considering the dangers that may result from the exercise of poor surgical judgment, but a simple method of treatment may be instituted and carried out with safety if the established surgical principles are observed.

Occasionally we see some serious complication or fatality resulting from an abscess that has been neglected or badly treated. The dangerous conditions which may result from an improperly treated abscess are lymphædema, lymphangitis, adenitis, erysipelas, cellulitis, septicæmia and pyæmia. Any one of these conditions may develop with amazing rapidity, producing an overwhelming toxæmia and death. Every effort of the tissue-cells is to localize the infection and to maintain localization. In the treatment, from the beginning, the method employed should be directed toward aiding localization.

Abscess may occur in any tissue of the body and by extension of the inflammatory process invade tendon sheaths, joints, any of the body cavities, mucous surfaces, or blood-vessels. I have chosen for this article, superficial abscess only; that is, those occurring in the skin and soft tissues immediately underlying it. This will comprise abscess of the scalp, lips, face, neck, back, chest and abdominal wall, axillæ, groins, buttocks, and soft tissues of the extremities.

Acute superficial circumscribed abscess is the term used to designate a localized inflammatory process of the superficial tissues resulting from bacterial invasion, entrance of an extraneous substance or an injury causing tissue necrosis, and which is undergoing or has undergone suppuration. In its progress it advances toward the skin and after fully maturing ruptures, emptying itself of the purulent exudate that has been confined under pressure within its cavity.

PATHOLOGY

Etiology.—The cause of abscess is most often due to bacterial invasion of tissues. *Staphylococcus pyogenes aureus* and *Staphylococcus pyogenes albus* are the commonest microorganisms causing acute circumscribed abscess, but any pus-producing germ, such as the *Streptococcus pyogenes*, *Bacillus coli communis*, *Pneumococcus*, *Gonococcus*, etc., may be the cause. It sometimes happens that a local area of necrosis is produced by trauma, and occasionally a foreign body that has entered the tissues will produce a localized necrosis as the result of irritation. A hematoma in the soft tissues may also become infected and result in abscess formation.

Immediately upon the invasion of healthy tissues by bacteria, there is a migration of leukocytes from the capillaries into the tissues and simultaneously there is an exudation of serum into the tissues invaded and in a large area surrounding it. With the migration of the leukocytes into the inflammatory area there is also a proliferation of the connective-tissue cells and it is by these cells that the so-called "pyogenic membrane" is formed. Toxic substances, which are the products of bacterial activity, cause death of the tissue-cells and the bacteria and leukocytes themselves die off in great numbers. When the tissue-cells, leukocytes and bacteria die, they are acted upon by proteolytic enzymes and are liquefied. As the abscess is developing, countless numbers of leukocytes are invading the area involved and with the proliferating connective-tissue cells they are forming an encircling zone around the necrotic centre to confine it and to prevent the advancement of the bacteria into the healthy tissues. This outer zone of cells becomes so dense that the blood- and lymph-vessels are closed off and there is no communication with the lymph or blood stream from the cavity of the abscess after it has formed. Within the zone of leukocytes and connective-tissue cells there is formed a thick liquid substance—the pus—made up of serum, dead tissue-cells, dead leukocytes and dead bacteria. The inflammatory area assumes an ovoid shape, one pole being directed toward the skin. The skin immediately over the inflammatory area begins to rise and assumes a bright red color. Later it becomes smooth and shiny, and the centre becomes bluish and at one place there will appear a creamy spot. This creamy spot is the pus burrowing through the layers of the skin by following a blood- or lymph-vessel and is

referred to as "pointing" of the abscess. It is from this point that the abscess will "burst." With the bursting of the abscess there will be an escape of the pus which had been confined under pressure and there may escape at the same time, or later, a small mass which is termed "the core." This core is made up of necrotic, fibrous connective-tissue which has not liquefied, and fibrils extending from it to the abscess wall may hold it within the cavity for a few days.

When the abscess ruptures, the walls fall together and within a few days the inner layer of the abscess wall separates. After this necrotic layer comes away, the surface is bright red and bleeds easily. This tissue is formed by the capillary loops and connective-tissue cells which are advancing by growth toward the centre of the cavity and which will eventually obliterate it.

When the tissue is first invaded by the bacteria and up to the time of the localization, the bacteria, bacterial toxins and products of autolysis of the tissue-cells drain into the lymphatic system. The lymphatic vessels draining this area become dilated and the capillaries in the connective-tissue surrounding them become congested. Those in the skin can be seen as red streaks running toward the nearest group of lymph-glands. With the localization of the infection the streaking due to the lymphangitis gradually fades away but the lymphoedema surrounding the inflammatory area remains. The glands communicating with the lymph-vessels draining the part may be enlarged and tender. The inflammation may extend into the connective-tissue around the glands and the glands may become adherent to one another and coalesce. Suppuration may occur in a single gland or all the glands of the group involved. If suppuration of the glands takes place it is usually sometime after the abscess has matured, often as late as two or three weeks. Lymph-glands that do not suppurate may remain enlarged for a long period. The part the lymphatics play in infections has been fully discussed recently by W. J. Mayo.

The character of the pus varies somewhat according to the invading organism and the tissue involved, but it is usually a thick substance with a creamy yellow or yellowish-green color. Creamy yellow pus is more often due to the presence of the *Staphylococcus pyogenes aureus* or *albus*; green or greenish-yellow pus is due to the presence of the *Bacillus pyocyaneus*; pus of a dirty grayish color is

usually due to the *Bacillus coli communis*. Gas in an abscess cavity is often a product of the invading organism and the *Bacillus coli communis* is one of the organisms occasionally producing gas. Solid, semi-solid or flaky particles seen in the pus are pieces of necrotic tissue which have not liquefied.

SYMPTOMS

The symptoms may be grouped into (1) local, and (2) general, and are due to the toxic products (1) of the bacteria, and (2) of the tissue-cells in the area invaded.

Local Signs and Symptoms.—At first there is a sensation of itching and irritation of the area involved, which is soon followed by a sensation of tension and later by a throbbing pain. With the onset of the throbbing pain there is tenderness and beginning redness. The pain gradually increases and is continuous, and with this there is swelling and increased redness and an increase of heat of the part. Accompanying these changes there may be a partial loss of function. The red, swollen area is indurated. This induration is at first hardest over the centre with diminishing hardness toward the periphery of the inflamed area. With the progression of the abscess toward maturity, the centre gradually changes from a bright red to bluish in color and with the change in color the centre becomes soft. As the centre softens, the skin becomes thinner and more shiny. In this shiny area there will appear a yellowish spot. The appearance of this spot is the pointing of the abscess. The abscess is now fully matured and will go on to rupture unless it is incised. When the abscess “bursts” or when it is incised, the pus will escape freely until the pressure within the cavity is relieved. With the escape of pus there is relief from pain and the function of the part slowly returns. The abscess wall gradually softens and the cavity is obliterated by the process of healing. With the healing the color of the part slowly returns to normal, but a red, indurated area will remain for a while at the site of the abscess cavity.

Constitutional Symptoms.—The constitutional symptoms accompanying an abscess are due to bacterial toxins, the toxic substances produced by tissue-cell autolysis, and in some instances bacteria themselves gaining entrance to the general circulation. The degree of toxæmia is dependent upon several factors; namely, the virulence

of the invading organism, the local resistance of the tissue-cells, the general resistance of the body cells—any one of which may be a factor in determining the ability to localize the infection—and, in some instances, the size of the area involved.

The commonest symptom, and one that comes soon after the onset of the infection, is fever, which may be preceded by sensations of chilliness or a chill. The fever is usually only one or two degrees above normal, but it may be quite high. A high fever may not indicate a severe infection and a severe infection which may terminate fatally may only show a moderate rise of temperature. The fever accompanying an abscess is most often a guide in determining whether a sapræmia, a septicæmia or a pyæmia is present.

Sapræmia usually accompanies circumscribed abscess. It is a condition where the organisms are in the abscess cavity but do not escape into the blood and the fever is part of the general reaction to the bacterial toxins or autolysates. There is an initial rise of the body temperature to its height, usually not higher than 102° F., and a gradual return within a few days to normal, where it remains. Septicæmia may follow sapræmia. It is due to a failure on the part of the tissue-cells to completely localize the infection, allowing the bacteria to gain entrance to the blood stream; or it may be due to rupture of the abscess into the deep tissues, allowing the pus to run along fascial planes, tendon sheaths, etc. The fever rises to 102° or 103° F., or higher. During the morning it may drop one and a half degrees but it rises again toward evening; being remittent in character. In pyæmia the bacteria are not only in the tissues primarily invaded, but also in the surrounding tissues, and the blood-vessels in this area become thrombosed. From the thrombosed vessels septic emboli and bacteria may reach other tissues, such as the heart, lungs, spleen, kidneys, liver, brain, etc., where new abscesses will be formed. The onset is characterized by a sudden chill and fever, and may follow sapræmia or septicæmia. The fever precedes or accompanies a chill. It rises to 103° or 104° F. After the chill there is a sudden drop in the temperature to normal or below and the patient is in a profuse sweat and shows signs of marked weakness. After several hours, the fever again rises to about 103° F., and prior to or accompanying the next chill there is a jump of one or two degrees. The chills may come every day or two, or there may be several each

day. Their occurrence is often significant of new abscess formation. With the progression of the disease, the patient becomes more septic. The disease runs its course in about two or three weeks and usually terminates fatally if numerous secondary abscesses form, if there are pulmonary infarcts which become purulent, if bronchopneumonia occurs, or if there is extensive thrombophlebitis.

DIAGNOSIS

There should be no difficulty in diagnosing a superficial abscess by the signs and symptoms already mentioned, but the local signs and the subjective and objective symptoms should be studied to determine if the infection has become localized, which is so important to consider in outlining the treatment. The temperature in all cases of abscess should be watched, as its character will aid in diagnosing sapræmia, septicæmia or pyæmia. If septicæmia or pyæmia is present, repeated blood-cultures should be made in an effort to isolate in pure culture the organism causing the infection.

TREATMENT

Most abscesses will require local treatment only, but if there are signs and symptoms present of sapræmia, septicæmia or pyæmia, the patient must also be given constitutional treatment.

Local Treatment.—The local treatment has been divided by Cheatele into (1) preventive, (2) palliative, (3) operative, and Pfahler has recently suggested an abortive treatment.

Preventive Treatment.—In abscess formation, even though the abscess be small, there is always a possibility of the occurrence of secondary abscesses, septicæmia, sapræmia or pyæmia. It would be most desirable to have some ready means to prevent such progress of the infection. Attempts have been made to kill the organisms in the primary field of invasion by (1) injection of antiseptics, (2) injection of vaccines, and (3) injection of antitoxic serums. None of these methods has proven successful and more can be done by local and constitutional treatment than any other method available.

When the patient first comes under observation a urinalysis should be made to determine if there is a glycosuria and repeated examinations of the urine should be made to watch for this condition while the patient is under treatment. The amount of the blood-sugar

should also be determined and it should be watched to see if it goes above normal. It has been recognized for a long time that boils and carbuncles occur frequently in diabetics, and Pfahler has noticed the occurrence of boils and carbuncles immediately following an excessive amount of sugar taken in the diet without producing an increase in the blood-sugar or a glycosuria. When a patient presents himself for treatment for a boil or a carbuncle he should be advised to reduce the amount of carbohydrates in his diet in order to prevent the occurrence of others.

Palliative.—The inflamed area should be thoroughly cleansed by gently washing the surface with a warm solution of green soap. This is best done with balls of cotton; rough gauze or a brush should never be employed. After the part has been thoroughly cleansed, it is shaved. The treatment now should be directed towards localization until the abscess has matured. The treatment that will aid mostly in localizing the abscess is the application of heat and moisture. This is best accomplished by the use of large, hot fomentations, kept on continuously, but changed at frequent intervals. The solution most often used and one that is easily prepared, and which is almost always at hand, is the saturated solution of magnesium sulphate. Morrison has suggested a solution that is even more hygroscopic and much more effective in withdrawing the serum from the tissues. It is made as follows:

R	Magnesium sulphate	40 ounces
	Boiling water	30 ounces
	Glycerine	10 ounces

(This is sterilized in the autoclave.)

Under aseptic conditions sterile dressings are wrung out of this solution, heated to 105° F., and applied to the surface, including an area well beyond the redness and swelling. Over this moist gauze there is applied a layer of oiled silk or thin rubber that extends well beyond the first layer. Then there is applied a layer of cotton or some other absorbent material. A bandage is loosely applied to hold the dressings in place. There may be placed over this one or two hot-water bags or an electric pad. Rest is very important and if the abscess involves one of the extremities, the part should be elevated. Elevation will favor lymphatic and venous drainage and will tend to relieve the throbbing pain.

Operative Treatment.—It might be stated as a rule, almost never to be broken, that incision should not be made before localization of the abscess. When the abscess has matured and pus has been located, it should then be incised and drained. When incision has been decided upon, the surface over the inflammatory area should again be thoroughly cleansed with a solution of green soap. Following this the surface should be bathed off with alcohol and ether to remove the moisture and soap. When the surface is dried, a 1 per cent. solution of picric acid in alcohol, or tincture of iodine may be applied as a skin antiseptic. For small abscesses the surface may be sprayed with ethyl chloride to obtain anæsthesia, but for large abscesses and abscesses in children, it is best to administer an inhalation anæsthetic of nitrous oxide and oxygen. The injection of a solution of novocaine to produce local anæsthesia is not advisable on account of the possibility of spreading the infection, but in some locations regional anæsthesia may be employed. Under aseptic conditions an incision is made over the thinnest place in the skin covering the abscess. If possible, it is made in one of the natural folds of the skin, but with care that important blood-vessels or nerves are not divided. The size of the incision should be large enough to allow complete evacuation and packing of the abscess cavity. After the incision is made, the pus will escape freely at first, then under gentle pressure the remainder can be expressed, or with the edges of the wound retracted, small gauze swabs or sponges may be used to gently wipe out the cavity. With the abscess cavity empty of pus, there is no need of a drainage tube. The cavity is packed tightly with plain or iodoform gauze (Frontispiece, *a* and *b*). The gauze allows for drainage of serum but it is not placed there for this purpose. The object in packing the cavity tightly with gauze, is (1) to prevent the walls of the abscess from collapsing and closing off or forming pockets that will confine collections of pus, and (2) to promote a further invasion of the area by leukocytes. After the abscess cavity has been carefully packed, a dressing moistened with warm magnesium sulphate solution or Morrison's solution is again applied and changed in the same manner as before. The gauze is not removed for forty-eight or seventy-two hours and only then if it comes away easily. No traction should be made upon it, as it will separate; adhering to it will be the necrotic tissue that formed the inner layer

of the abscess wall. The abscess cavity is not re-packed as a rule, but it may be lightly packed with gauze strips wrung out of magnesium sulphate solution or filled with a mixture of balsam of Peru and castor oil. The hot fomentations are continued until healing is well advanced.

Abortive Treatment.—Pfahler advises massage and states that the massage is not painful if begun at the earliest sign of a lesion. The area should be thoroughly washed with soap and then thoroughly massaged with mentholated vaseline for five or ten minutes three or four times daily. This, however, is contrary to the view held by most surgeons that an acute inflammatory area should not be massaged.

Certain abscesses, such as palmar abscess, tuberculous and typhoid abscesses, will require special treatment, and these have not been considered in the above. Certain large phlegmons might best be treated by the use of the Carrel-Dakin method.

Constitutional Treatment.—Rest, a good nutritious diet, the free intake of liquids, laxatives or enemas, and bathing, are usually all that is necessary. Where there is a high fever or a severe toxæmia, the constitutional treatment is of the greatest importance. Sponge baths should be given every few hours until the fever is reduced to 102.5° F. The patient should be on liquid diet, and on a sufficient quantity to insure a large liquid intake. For pain and restlessness, sedatives and morphine may be given. Stimulants, such as whisky, digitalis, strychnine, etc., should be given when indicated. If there is nausea and vomiting, water, normal salt solution, or glucose solution and stimulants may be given by rectum. Transfusion of blood is one of the most valuable aids we have in combating infection and in septicæmia or pyæmia, 300 to 500 c.c. of blood may be given every three or four days, or daily if indicated. Methylene blue, gentian violet, mercurochrome, etc., have been used in an attempt to sterilize the blood and tissues where organisms have been found in the blood stream, and some very striking results have been reported following their use, but it has not been established which organisms are destroyed by each dye, nor has this therapy advanced to the place where it can be used with safety. For localized abscess it is a question whether these dyes should be injected into the circulating blood, as the experiments of Cheatle have proven that the cavity does not communicate with the lymph or blood stream and that the dyes will

not reach the area where the organisms are living. Some of these dyes might prove to be effective in killing off the bacteria in localized abscess if injected directly into the inflammatory area.

CONCLUSIONS

(1) The effort on the part of the tissue-cells in abscess formation is to localize the infection and to maintain the localization by walling off the abscess cavity.

(2) In the treatment the method employed should be directed toward aiding localization. This is best accomplished by the use of warm, moist, sterile dressings.

(3) When the abscess has matured, it should be incised under aseptic conditions and its contents evacuated.

(4) Gauze packs tightly placed within the abscess cavity will prevent the closing off of pockets containing pus and will stimulate a further invasion of leukocytes during the time the necrotic wall is separating and until healing has begun.

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THE SURGICAL TREATMENT OF GASTRIC AND DUODENAL ULCERS

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SURGICAL TREATMENT

THE surgical treatment of duodenal and gastric ulcers has been viewed and commented upon from several angles. The variable phases in the treatment depend directly upon the obscure etiology of the condition. Pathologically, duodenal and gastric ulcers present a similar process. Ivy and Shapiro have produced gastric ulcers on the basis of local anaphylaxis to foreign proteins.

Since the practice of subtotal gastrectomy, much more has been learned from the gross and microscopic study of specimens than was possible from necropsy material. Konjetsky recently reported the detailed histologic study of a large number of duodeni and stomachs removed at operation. From this study there is no evidence that the defect in the mucous membrane depends upon nutritional disturbance, a sequel to changes in the smaller blood-vessels. On the contrary, where differentiation is possible *inflammatory mucosal changes* predominate as the outstanding microscopic picture. In every case the development of the ulcer was the result of a definite inflammatory destruction of the mucosa. In many places the normal surface presented evidence of healed ulceration, but frequently the latter was limited to the superficial layer. The inflammatory reaction was most advanced in the antrum of the stomach and in the bulbus duodeni. In brief, all cases showed a more or less diffuse chronic gastritis or duodenitis in various stages of development. This is in common with the findings of other observers. Whether the extensive inflammatory changes develop primary or secondary to the appearance of the ulcer is still unsettled.

In from 5 to 10 per cent. of the cases the ulcers were multiple; and in some instances the coexistence of an ulcer in the stomach and in the duodenum was observed in the same specimen. The appearance successively or simultaneously of two or more ulcers in a patient has been termed clinically "the spontaneous double ulcer."

The conception of ulcer genesis on a basis of pyloric spasm was first sponsored by Mickulicz in 1897. The great frequency of pyloric spasm both in the nursling and in the adult is well known to every clinician. The pyloric spasm interferes with the normal emptying of the stomach and brings about a definite state of gastric retention. Intermittent or continuous spasmodic contractions also occur at other sphincter sites, *e.g.*, spasm of the cardia which produces an œsophageal dilation, and spasm of the sphincter papilla (sph. Oddi) causing dilation of the common and hepatic ducts. Heidenhain is a strong supporter of the pyloric spasm hypothesis as one of the chief causes in the development of gastric and duodenal ulcers.

The neurogenic theory as the cause of the occurrence of duodenal and gastric ulcers must be ignored, although it is of distinct interest from a surgical viewpoint.

This brief discussion of a few factors that are related to the genesis of gastric and duodenal ulcers is presented as evidence of the unsettled status of the entire problem.

At the present time there appears to be a definite tendency toward radical surgery in all ulcers, but since their etiology is far from settled the type of operation cannot be standardized. In the light of our present knowledge no attempt should be made to use one certain operation for the treatment of every condition. Only practical experience and long clinical end-results can form a basis for rational treatment. The type of operation that is to be performed depends upon a number of factors, of which the most important are (1) the location and character of the ulcer, (2) the general condition of the patient, (3) the possibility of the malignancy of the ulcer, (4) the degree of gastric acidity.

In simple ulcer of the duodenum, gastro-enterostomy gives me excellent results. In a series of over one hundred gastro-enterostomies, there were 90 per cent. cures, and 1.8 per cent. later developed jejunal ulcers. Pyloric exclusion was not used in the above series in combination with the gastro-enterostomy. Christian Bull, recently (Oct., 1925) in a critical analysis of ninety-four cases and X-ray follow-up, similarly notes that better results were obtained without pyloric exclusion. Additionally, a number of Continental surgeons who formerly routinely added some type of pyloric exclusion to the gastro-enterostomy have long since abandoned it. Excision of the

duodenal ulcer is not made a part of the surgical procedure because of the possibility of reflex spasm of the pylorus from the resultant scar. Bull, quoted above, makes the same observation, and in his cases notes that excision of the ulcer gives the least favorable results, all of these cases having been cited as unimproved.

Gastric pyloric ulcers are readily cured by simple gastro-enterostomy. In cases of healed duodenal or gastric ulcers with constriction of the pylorus, Finney's pyloroplasty has given me most excellent results, and in this type of case pyloroplasty is, I believe, the procedure of choice. The operation must be performed without clamps, as the application of the latter to the wall of the duodenum is not without danger of necrosis as occurred to me in one patient.

In the saddle type of ulcer, and ulcers of the lesser curvature, which are occasionally multiple, resection is the operation of choice if the patient's condition allows it. Gastro-enterostomy may be indicated, however, if the patient is old or debilitated or if resection cannot be performed without great risk on account of extensive adhesions.

Bull notes that the results of his operations are always better after gastro-enterostomy than after resection, this with no regard to the localization of the ulcer. Finsterer, who routinely removes the greater part of the stomach in both gastric and duodenal ulcers, claims clinical cures in all his cases.

TECHNIC

Operation is carried out under general anæsthesia, using nitrous oxide and oxygen, and ether. A considerable number of gastro-enterostomies and resections have been performed under local and splanchnic anæsthesia with no particular difficulty. The mechanical procedures on the stomach and intestines can be done with very light anæsthesia. A right pararectus incision is used, and the gall-bladder and appendix are first inspected. If the ulcer be not readily found, the lesser peritoneal cavity (bursa omentalis) should always be opened. Inflammatory changes are not uncommon here and it is possible to entirely overlook an ulcer on the posterior surface of the stomach unless this is made a part of the surgical procedure. Usually, the exposure of the bursa omentalis is most easily effected through the gastrocolic omentum; occasionally adhesions make it difficult.

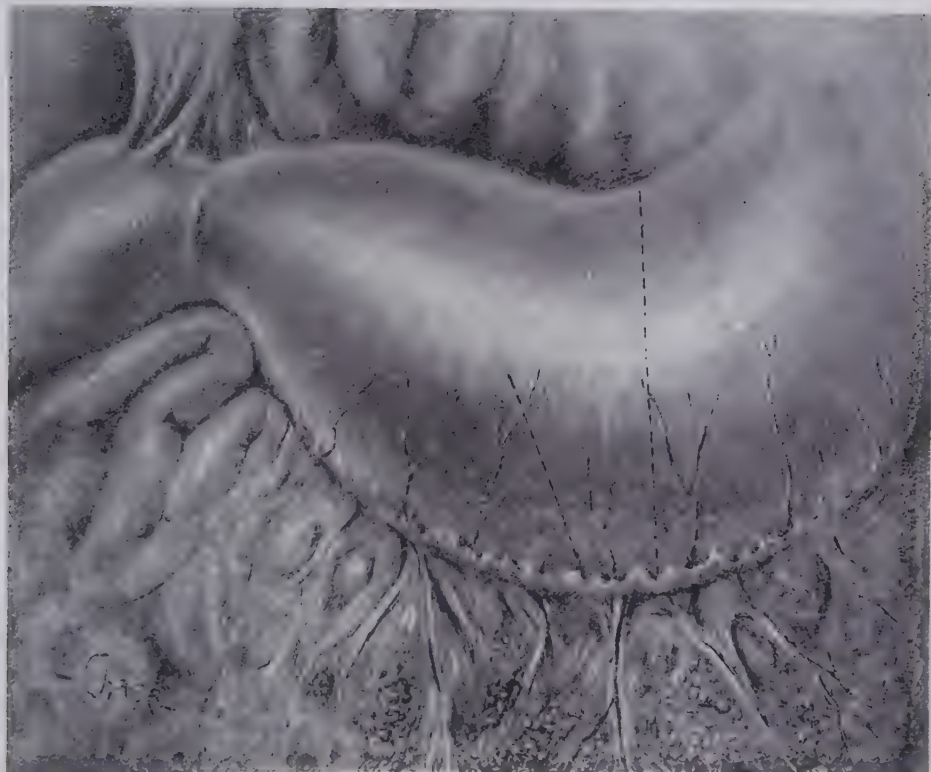
In almost all cases where gastro-enterostomy is performed the

classical posterior no-loop operation is the procedure of choice. The incision in the mesocolon is usually made some distance above the transverse colon and as near as possible to the vertebral column. The edges of the mesocolon are fixed to the stomach by a number of sutures before the anastomosis is begun. I believe it to be a matter of indifference whether fine silk or fine chromic catgut is used for the peritoneal approximation. Personally I feel that it is safer to use silk for the peritoneal suture and hard tanned catgut, size O, with the needle swedged upon the end of the suture, for the inner layer or layers. Care must be taken to bring about absolute apposition of the mucous coat, so that no gap remains between the stitches. The strip of mucous membrane presenting at the opening should always be excised. This gives a much neater union, and there is less danger of the formation of a gap in which a suture might persist and act as a foreign body.

In recent years I have not been doing a strictly no-loop operation in pyloric and duodenal ulcers, but place the opening two or three inches from the duodenojejunal flexure. The experience of operating upon a number of gastrojejunal ulcer cases where the no-loop operation had been the primary procedure led me to abandon the strictly no-loop operation. No ill effect has been noted since adopting the use of a two- or three-inch loop. Walton believes that we have been obsessed with the idea of the value of the no-loop anastomosis owing to the evil effects which unquestionably follow the use of a very long loop. The stoma is placed from right to left, from the greater curvature upward toward the left. The distal end of the jejunum is approximated to the greater curvature. The anastomotic opening is usually made three to three and one-half inches from the pylorus.

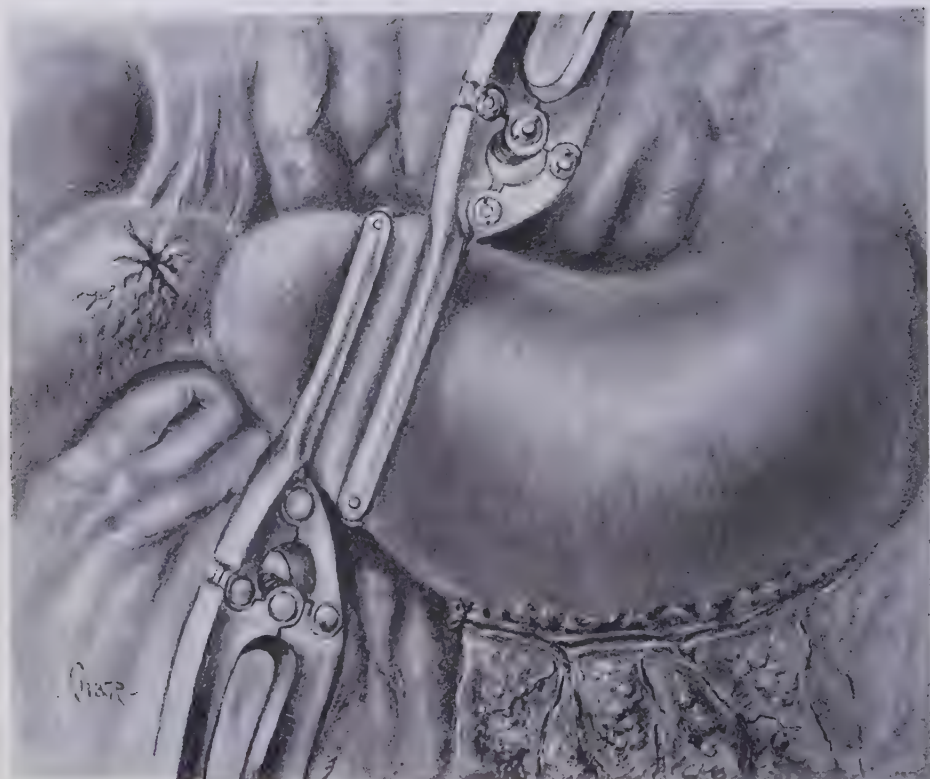
In the technic of resection the most important step is the satisfactory mobilization of the stomach. As a rule the removal of the stomach is begun at the duodenal end. It is important that the line of resection be carried out in normal stomach wall; usually about half of the stomach is removed. The duodenum is crushed with a Payr's clamp, a silk ligature tied in the groove and the end inverted with interrupted sutures, preferably of the mattress variety. It is important also in the inversion of the duodenum that its closure be effected in healthy tissue; if necessary, a part of the stomach even proximal to the pylorus may be utilized for the site of the inversion.

FIG. 1.



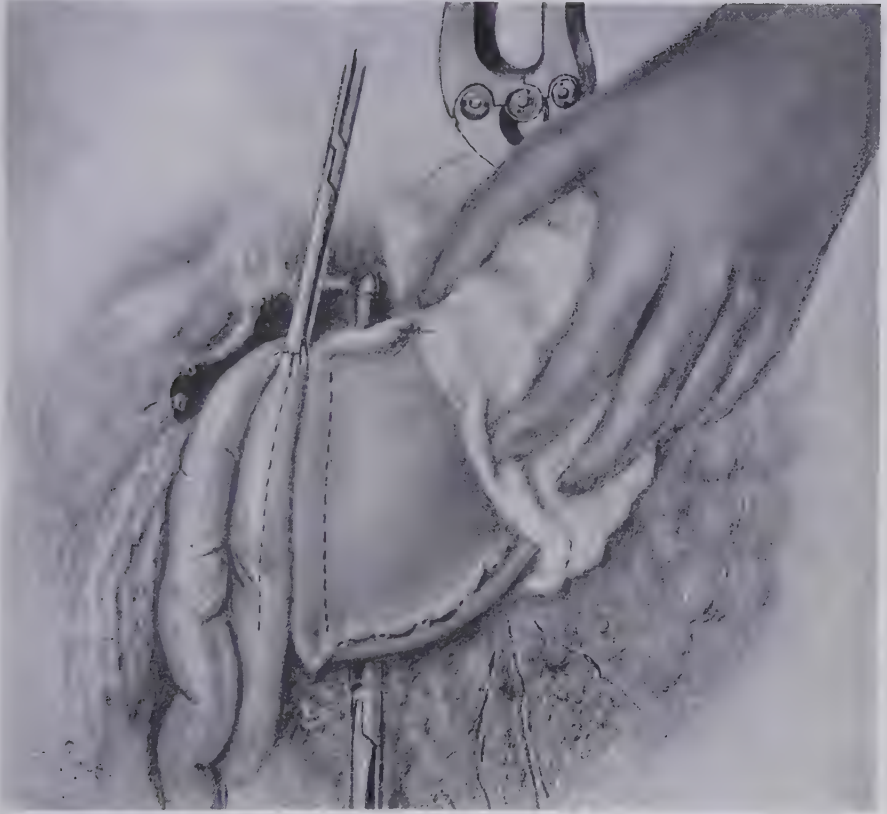
The short dotted line represents the site of a posterior gastro-enterostomy, the long dotted line is the line of division of the stomach for resection.

FIG. 2.



The line of division for resection when there is extensive induration of the duodenum; modified from Balfour.

FIG. 3.



The Balfour anastomosis. Approximation of a sixteen-inch loop to the end of the stomach and in front of the colon with the posterior suture begun before the stomach is resected. The part of the stomach to be resected is held to the left. The first row of sutures is placed before the stomach is removed.

(Fig. 2.) Occasionally one is able to approximate the lumen of the stomach and duodenum without tension; in this case continuity is reëstablished by the Billroth I, but usually a dangerous angle is formed and the suturing is insecure. When possible the resection is completed by a posterior gastro-enterostomy; or the entire end or the lower half of the transverse section of the stomach is anastomosed to a short retrocolically placed jejunal loop in the usual manner. The Balfour modification of the Polya operation has also given me satisfactory results. (Fig. 3.)

POST-OPERATIVE TREATMENT

Following either gastro-enterostomy or resection the patient is given a Murphy drip by rectum, and, if indicated, subcutaneous introduction of salt solution, either at eight- or twelve-hour intervals, or continuous hypodermoclysis, depending upon the condition of the patient. Transfusion is resorted to if necessary. Morphine in small doses should be given if pain and discomfort are marked during the first twenty-four hours.

The use of ice, or milk, unless peptonized, is absolutely interdicted as a part of the post-operative treatment. In the absence of nausea or vomiting, hourly doses of hot water or tea are administered at the end of the sixth hour, so that the patient in the course of a day receives about 200 c.c. of fluid. This restriction of fluids by mouth is compensated by rectal and subcutaneous injection. From the third to the fifth day the quantity of fluids is increased from 600 to 800-1000 c.c. On the third day broiled steak may be chewed by the patient and the pulp rejected with extremely beneficial results. This brings about all physiological processes and is therefore superior to the ingestion of broth or beef tea. On the fifth or sixth day, I begin with soft pulpy food.

Gastric lavage is occasionally necessary after gastro-enterostomy or resection if nausea or vomiting persists. The fluid obtained is often blood tinged. (The latter may have its source in either a remaining ulcer or from the suture line.) It is frequently possible to avoid the use of gastric lavage by the administration of a Seidlitz powder; if the latter fails to afford relief, resort is then made without hesitancy to the stomach tube. The lavage must be carried out under low pressure and only a small quantity of fluid (200 to 400 c.c.) used.

It is always well tolerated, and the result most gratifying. No adverse effect has been noted in my experience of its use.

It is noteworthy that in gastric resection of the Billroth II type, lavage is rarely necessary. It is obvious that in the latter type of operation the emptying of the stomach takes place more readily than in Billroth I or after a gastro-enterostomy.

COMMENT

Considerable variation of opinion is expressed by able observers concerning the possibility of malignant change in an existing ulcer. V. Haberer states that it occurs in 5 per cent. of cases. Other opinions vary from practically negative to as high as 30 per cent. Cole states that the grafting of malignancy on a previous ulcer is a most unusual event, basing his opinion upon the result of continued X-ray studies.

The operation of gastro-enterostomy should not be shunned on account of the present wave which favors gastric resections in all types of gastric and duodenal ulcers. I cannot subscribe to the enthusiasm for the radical method which has now so many advocates. The results following gastro-enterostomy are certain in the majority of chronic duodenal and pyloric ulcers; patients are relieved of symptoms and remain well as they are followed from year to year.

The outstanding complication of gastro-enterostomy is the development of a gastrojejunal ulcer. This crippling lesion has caused a considerable number of surgeons to adopt gastrectomy as the operation of choice in all gastric and duodenal ulcers. While the mortality of gastrectomy is surprisingly low, and the immediate results most satisfactory, it does not absolutely eliminate the incidence of gastrojejunal ulcer, and is not without other dangers. If the occurrence of jejunal ulcers is dependent upon acidity, at least two-thirds of the stomach must be removed at operation. Radasch, in a study of the histology of the stomach, found that the acid cells began at the cardiac end of the stomach and extended for about two-thirds of the distance of the lesser curvature and three-fourths of the distance of the greater curvature, ending in a very sharp line at the above points. If a gastrectomy be performed in order to produce a certain anacidity the greater part of the stomach must be resected.

Gastrojejunal ulcers predominate in the male and are most commonly observed after pyloric and duodenal ulcers. Mandel and

Holbaum have never observed such an ulcer following an ulcer of the middle of the stomach. In Walton's series of twenty cases, only one gastrojejunal ulcer developed after an ulcer of the lesser curvature; the latter instance was associated with a very high gastric acidity.

It has been generally assumed that gastrojejunal ulcers do not occur after gastrectomy but there are reports appearing that resection of the stomach does not entirely eliminate this hazard. Probably the incidence of jejunal ulceration is less after resection than after gastro-enterostomy. Walton reports two cases following partial gastrectomy by other surgeons. Similar incidents are reported by Beer. V. Haberer has abandoned the Billroth II in favor of Billroth I, as gastrojejunal ulceration was so common after the former operation. Wright also reports two similar cases and notes that up to the present time gastric resection had been reserved for gastric carcinoma. It is only in recent years that gastrectomy has been carried out in the treatment of peptic ulcers, and jejunal ulcers are now beginning to appear. Walton states there is doubt that this serious complication is entirely eliminated by the substitution of the more dangerous operation of partial gastrectomy. Denk, in his study of 301 jejunal ulcers, found six proved cases and ten suspicious cases following gastric resection. Reichel observed two cases after total resection of the stomach. Finsterer mentioned seven gastrojejunal ulcers following partial gastrectomies which had been performed by other surgeons. The treatment of gastrojejunal ulcer consists of a gastrectomy beyond the point of anastomosis and re-anastomosing the jejunum to the stomach. Finsterer recently has given up the anastomosis of Roux, because of two recurrences following the latter type of operation.

Hurst puts special stress upon the late complications which follow gastrectomy and has even claimed that it may be followed by pernicious anæmia. He states that he knows five such cases where this complication occurred. Whether or not these claims will be substantiated it is evident that removal of large portions of healthy stomach may be followed in the future by grave complications. In spite of statistical evidence showing a very low mortality in the hands of the average surgeon, Walton says that the mortality in gastrectomy will be higher than the combined mortality of gastro-

enterostomy and the incidence of gastrojejunal ulcer after such an operation.

In 1921 Clairmount observed before the German Surgical Congress that there was no great difference in the end-results between gastro-enterostomy and the various types of resection. In the beginning surgeons began to treat these ulcers by gastro-enterostomy, then turned vigorously to gastrectomy, and now the pendulum has swung back to gastro-enterostomy. Gastro-enterostomy is not a panacea but the results are so good, the mortality so small, that except in instances noted under certain types of gastric ulcer, gastro-enterostomy is still the operation of choice in the majority of ulcers.

SURGICAL CLINICS FROM THE BROAD STREET HOSPITAL, NEW YORK

(1) Pathological Fracture of the Humerus Due to Carcinoma Metastatic from a "Silent" Growth in the Oesophagus.

(2) Rupture of the Liver.

(3) Pistol-shot Wound of the Colon and Kidney.

(4) Traumatic Synovitis of the Knee—Aspiration Treatment.

(5) Torn Internal Semilunar Cartilage of the Knee.

By WALTER M. BRICKNER, M.D., F.A.C.S.

Attending Surgeon

and

HENRY MILCH, M.D.

Assistant Surgeon

(1) PATHOLOGICAL FRACTURE OF THE HUMERUS DUE TO CARCINOMA METASTATIC FROM A "SILENT" GROWTH IN THE OESOPHAGUS

Patrick M., aged thirty-eight, was struck in the right shoulder by a sliding car-door. Thereafter he had moderate pain, but no loss of function, and he continued at his work as a railroad guard until, two weeks after this mild trauma, while putting his right hand in his pocket, he felt something snap in his arm, which fell useless. Brought to the hospital the same day, June 12, 1925, he was admitted to our service in great pain.

The report of the case as telephoned to the attending surgeon established at once a diagnosis of pathological fracture of the humerus. The upper end of the right arm was found swollen and tender, but there was no other deformity. No effort was made to elicit crepitation or to test motion or mobility, lest by these manipulations the bone fragments, apparently not displaced, should become separated. An immobilizing plaster-of-Paris cap was bandaged to the arm.

Röntgenograms on the day of admission (Fig. 1) supported the tentative clinical diagnosis of bone neoplasm and negatived the other possibilities—gumma, cyst, osteitis fibrosa, Paget's disease. The picture shows, a little below the head of the humerus, a much circumscribed medullary process (absorption) breaking through the cortex, with no periosteal growth or apparent invasion of the soft tissues. It did not give the appearance of a sarcoma (*vide infra*). It seemed to us most likely that the tumor was metastatic (carcinoma?, hypernephroma?); and, accordingly, painstaking search was made for a primary growth.

The man's previous history was negative and his signs and symptoms were limited to the affected arm. He was in fairly good health and had not noted any loss of weight or strength. He was, however, rather pale (hemoglobin, 60 per cent.). Repeated physical examinations, including lungs, nasopharynx, kidneys, prostate, bones and skin were entirely negative—except for a small lipoma between the scapulæ. There was no sebaceous cyst (which, rarely, becomes

carcinomatous) and no history or scar of one that had been removed. Röntgenograms of the chest, the head and all the other bones were negative. The urine showed no albumin, blood-cells or Bence-Jones bodies. The blood Wassermann reaction was negative, as also were examinations of the stools.

A röntgenogram on June 23rd showed that the neoplasm was growing rapidly and had extended almost to but not into the shoulder-joint and also, apparently, not yet into the soft parts. In the face of failure to find a primary tumor or any other metastasis, it was decided to give the patient the possible benefit of removal of the growth in spite of the strong suspicion that it was metastatic.

Operation was therefore performed on June 25th. Through a free incision there was readily exposed the softened, fractured bone and a small area of infiltrated muscle tissue. A piece of the growth, removed for frozen section diagnosis, was reported by Dr. M. J. Fein, the hospital pathologist, "sarcoma, type undetermined." The upper third of the humerus, including about two inches of the shaft below the growth, was then at once removed *en bloc* with muscle and tendon attachments (Fig. 2). After freely swabbing out the wound cavity with alcohol (to destroy and to remove loosened tumor cells), a sufficiently long and stout osteoperiosteal graft from the crest of the right tibia was driven into the medullary cavity of the humerus below and mortised into the glenoid surface of the scapula above (Fig. 3). Closure without drainage. Both wounds healed promptly, *per primam*; the transplant remained in place; and the patient was soon encouraged to use his forearm and hand.

Several days after the operation Doctor Fein reported that the tumor was not a sarcoma, as his hasty frozen section examination had led him to believe, but an epidermoid carcinoma. This was confirmed by other pathologists. Thereupon further, unavailing searches for a primary growth were made. The lipoma was removed but no suspicious area was found in it. Early in August, about eight weeks after admission, the patient mentioned almost casually in the course of one of his periodic cross-examinations, that for several days he had experienced increasing difficulty in swallowing solid food. A barium-meal röntgenogram of the œsophagus, then made, showed an almost complete obstruction at the level of the fourth thoracic vertebra (Fig. 4). Œsophagoscopy, by Dr. Rudolph Kramer, demonstrated a large growth 28 cm. from the incisor teeth; and a fragment removed therefrom showed epidermoid carcinoma of the same type as the bone growth.

With these findings the case was complete from the diagnostic side. The next problem was what should be done further for the unfortunate man. Resection of the thoracic œsophagus, a formidable procedure, and usually a fatal one, was not to be considered for a metastasising growth. Gastrostomy we also rejected: It does not stay the progress of the disease and, unless obstruction is complete, does not prolong life; this man could swallow liquids and semi-liquids without distress, and, more than that, could not be fed through a gastric fistula. The appearance of the growth showed that attempts to palliate by the passage of dilators would be both dangerous and futile. To use radium seemed to us a mere formula—a last resort that would have accomplished little or nothing. We decided our course of action from other considerations. The man had left his wife and children in Ireland to earn a living for them in this country. It seemed the most humane thing to let him end his days with them rather than in an

FIG. 1.



Patrick M. Metastatic carcinoma of the humerus producing pathological fracture. Note that the growth appears quite circumscribed. There is bone absorption but no bone production, bone expansion, periosteal growth or cystic degeneration.

FIG. 2.



Patrick M. Radiographs of the same growth two weeks later, after removal with some of the attached soft parts. The second picture shows the growth split open. Note the rapid extension of bone destruction almost to the articular surface.

FIG. 3.



Patrick M. Osteoperiosteal transplant from tibia to replace resected portion of humerus.

FIG. 4.



Patrick M. Carcinomatous obstruction of the thoracic œsophagus.

institution or in a strange lodging-house on the other side of the ocean. His employer, the Hudson and Manhattan Railway Company, which paid his hospital bill, also generously gave him a sum of money, with which, and a letter to a local surgeon, he returned to his home in Ireland. There he died a few weeks later.

Bone metastasis of carcinoma most often occurs from growths in the breast, prostate, thyroid or adrenal. It is uncommon from cancer of the stomach or intestine and is probably rather rare from the œsophagus. It will be recalled that the röntgenogram of the chest of this patient showed no glandular enlargements or abnormal mediastinal shadow and that during several weeks of observation he gave no sign or symptom of a lesion in his alimentary organs. As Virchow, Ribbert and other pathologists have pointed out, however, cancer of the gullet may be latent, symptomatically, and discovered accidentally on the autopsy table. This case demonstrates, therefore, that in spite of the comparative rarity of such a type of metastasis, it is worth while, in seeking a "silent" primary growth, to make a complete X-ray examination of the digestive tract—as also, if need be, sigmoidoscopic, cystoscopic and pyelographic examinations.

To make a diagnosis of pathological fracture in a case such as this is relatively simple. In fact, it is established on the mere history. If a person suffers a fracture without external violence or after a trivial trauma, the presumption is that osteoporotic changes have taken place as a result of some pathological involvement. The most common of these causes, exclusive of bone destruction by osteomyelitis, we have mentioned above. Their differentiation can usually be made röntgenographically. Indeed, skilled interpretation of the röntgen film is quite as important as, and often more reliable than, the histologic report; for the latter is often disputed by experts or refuted by the course of the disease. The differentiating röntgen appearances of various bone affections were described by one of us¹ several years ago.

Medullary sarcoma is characterized by pronounced rarefaction of the bone, and expansion and shell-like thinning out of the cortex; there is no periosteal shadow while the tumor is within the bone, and there may be none even if it breaks through the bone. Periosteal sarcoma is characterized by a blotchy or fringe-like periosteal shadow which may appear to radiate from the bone like swirls in a sand-storm, fading out into the fainter shadow of the tumor mass. While

this appearance is sometimes mistaken for that of the periostitis seen in syphilis, the latter is to be distinguished by the fact that, narrow or wide, it hugs the bone and is fairly sharply edged. Moreover, syphilitic periostitis is often associated with ostitis, marked by the dense shadow of bone production, centripetal or centrifugal, or both. In the ossifying process periosteum and cortex may fuse into a bony mass, appearing in the film as a uniformly dense, structureless shadow. In its early phase "sclerosing sarcoma" of the bone may much resemble lues in its röntgen appearance. Bone syphilis is essentially a productive inflammation. Sometimes, however, there is also associated bone destruction, and a gumma may thus cause a pathological fracture. It can be distinguished from sarcoma, carcinoma, and cyst by the absence of bone expansion and by the presence of the surrounding reactive ostitis and periostitis. Myeloma presents the same X-ray appearance as medullary sarcoma; it has a tendency to multiplicity and a predilection for the ends of the long bones, the ribs and the cranial diploë. Carcinoma appears in the bones, röntgenographically, in two forms. In one the picture is much like that of a central sarcoma, *viz.*, rarefied tumor area and thinning of the surrounding bone, without, however, the expansion of the bone shell so conspicuous in sarcoma. In the second form the bone appears irregularly eaten away, superficially as well as in the depth, and what bone structure is left in the tumor area appears spongy, porous, eroded, as in Fig. 2. In carcinoma one never sees reactive bone production.

Bone cysts, of various types histologically, present a picture much like that of endosteal sarcoma: Translucency; thinning and expansion of the cortex. As compared with sarcoma, however, the bony wall of the cyst is sharply outlined and the light area is often traversed by the shadows of trabeculæ. Trabeculæ are sometimes seen in giant-cell (central) sarcomata, and while, typically, they do not appear as sharp or as complete as in cysts, the differentiation of these two lesions röntgenographically may be difficult or impossible. The wall of the cyst is often the seat of a pathological fracture, but the film never shows it extensively absorbed or broken through as in sarcoma. The röntgen-ray differentiation of bone tumors, and its limitations, has been well discussed by Baetjer.²

The earlier a bone tumor is recognized, the more difficult is the

diagnosis of its type. Recourse may be had to biopsy, but with two very important provisos: First, that a frozen section be examined immediately, and second, that the surgeon be prepared and permitted to proceed at once with whatever operation is then decided upon.

In this case, upon the biopsy report of sarcoma, we elected resection rather than amputation. Even an interscapulo-thoracic removal of the extremity would have offered no better prognosis. Amputation rarely, if ever, effects a cure of medullary and subperiosteal osteogenic sarcomata. Such cases die within a few months from metastasis—usually in the lungs. MacGuire and McWhorter³ have showed that the presumed-to-be fairly benign giant-cell sarcoma is more often malignant than is generally supposed, not infrequently causing death after amputation from recurrence in the stump or metastasis in the lung. They found in thus malignant cases an increase of cellularity and mitosis and a decrease in the number and size of the giant cells.

(2) RUPTURE OF THE LIVER

Lacerations of the liver associated with some form of penetrating wound were fairly common during the war, but serious hepatic ruptures resulting from an injury that does not break the skin, compression fractures of the liver, are rather unusual.

Robert C., aged thirty, was brought to the hospital on April 25, 1925, at 4:30 P.M., after having been crushed between an elevator cage and the shaft. The house surgeon could find no evidence of any internal injury and instituted the usual morphine and heat treatment for his evident shock. On admission, the pulse-rate was 96 and the condition was reported as satisfactory. Two hours later, the patient suddenly became pulseless and was recognized to be in extremis. He was found cold and clammy, breathing rapidly and with a slight rise in temperature. Strangely enough, the pulse soon again became slow and of good volume. There was a small area of ecchymosis over the eighth and ninth ribs on the right side, with slight but persistent tenderness over the liver region. There were a definite fluid wave and shifting dullness in the flanks. The blood-pressure, which shortly before had been 90 systolic, now had dropped to 80, and it was decided that the patient presented urgent indications for exploratory laparotomy. As was expected, the abdominal cavity was found to be full of blood. With some difficulty there was exposed a large rent in the liver extending from the dome through the gall-bladder bed and the lower surface of the right lobe of the organ well back to the spigelian lobe. So extensive was the laceration that it was considered useless to attempt to control the hemorrhage by packing. By using large mattress-sutures of chromicized catgut on a blunt needle, the edges of the huge rent were approximated except at the portal fissure. During the operation,

the patient's condition became more and more precarious from hemorrhage. About two quarts of blood were sponged from the abdomen, filtered and injected intravenously. At the same time cardiac stimulants were administered and shortly thereafter an infusion of saline solution was given intravenously. Several gauze packings were applied to the still unsutured portion of the rent and the abdomen was closed. Death occurred within an hour.

This case presents several interesting points for discussion. The differentiation of the effects of shock and internal hemorrhage when they coexist offers one of the most difficult and at the same time most important problems in traumatic surgery. When either condition is present alone, it is fairly easy to recognize its essential features, but when the signs of shock are masked by the occurrence of a massive hemorrhage, as occurred in this case, the differentiation becomes exceedingly difficult. Vexing as this problem frequently is, its solution is made the more baffling in cases of liver injury by the fact that the pulse, which would ordinarily be small and rapid, is full and slow. It is rarely possible to definitely make the diagnosis of rupture of the liver. At best, the most one can say is that there exists an injury to an abdominal viscus or an internal hemorrhage probably due to an injury to the liver. However, if there is any sign pathognomonic of hepatic tear, it is the slow, full pulse which has been repeatedly observed in injuries to that viscus or the biliary pathways. What the exact mechanism of this bradycardia may be cannot be definitely stated. By some it has been considered as being caused by a blunt injury to the abdomen, but most authors are inclined to the opinion that absorption of bile salts, either from the exudate in the peritoneal cavity or by the hepatic veins directly from the lacerated surface, offers the more likely explanation. The bradycardia, an evidence of the medullary action of the absorbed bile salts, may continue for some time even in the presence of extremely severe hemorrhages. In such cases, pallor, the fall in the blood-pressure and the demonstration of free fluid in the abdominal cavity are of more significance than the character of the pulse. The determination that there is an internal, progressing hemorrhage establishes the operative indication, even if, as in this case, the lower danger limit of blood-pressure has been reached. Unfortunately, the outlook is poor whether operation is undertaken or not. Sixty to seventy-five per cent. of these cases are fatal in any event. There are, of course, instances of laceration of the liver recovering without operation, but

they are doubtless those in which the tear was comparatively small or in which it was effectually sealed by the interposition of omentum.

Occasionally subcutaneous injuries to the liver are caused indirectly, as by falling on the head or on the feet from some distance. For the most part, however, they are due to a direct compressive force exerted on the upper abdomen or the chest wall. The greater frequency of liver over spleen injuries in such compressive traumata must be explained by the association of two factors, the friability of the organ, due to its relative lack of elastic fibres, and its immobility.

As Krogius has shown, liver injuries may be divided into two main types: (1) "Compression" rupture and (2) "bending" rupture. In the former the line of rupture is usually in the direction of, while in the latter it is at right angles to, the traumatizing force. The injuries of the first group are usually deep and irregular lacerations, while those of the second group are superficial and more regular in outline. According to this classification, the case here reported would most probably belong to the group of compression ruptures.

The operative approach is best made through a right rectus-splitting incision. This permits adequate exposure and at the same time reduces the probability, as compared with transverse incisions, of post-operative herniation. Once the rent in the organ is discovered, temporary control of the bleeding may be obtained by simply digitally compressing the edge of the gastro-hepatic omentum in which the blood supply of the liver courses. Compression of these vessels may be continued for as long as forty minutes without doing any permanent damage. Wherever possible the individual bleeding vessels should be caught and ligated in the usual manner, but most frequently the surgeon is confronted with a diffuse venous hemorrhage which can best be controlled by packing. Plain gauze strips are used and no effort is made to remove them until at least the end of the tenth day, because the healing power of the liver is so retarded that an earlier attempt might result in fresh bleeding.

When the rent is small or, on the other hand, when it is so large that packing does not control the hemorrhage, suture should be undertaken. The problem connected with suturing the liver is that the stitches can with difficulty be prevented from cutting through the friable gland tissue. To avoid this, a great many suggestions have

been made. In the first place, only large, round, non-cutting needles should be employed and in placing the suture an effort should be made to include a portion of the fibrous tissue capsule of the liver in the bite. Deep mattress-sutures are less apt to cut through, on tying, than single stitches. A double stitch may be used, tying each end of the two strands over bits of fascia, muscle or fat, as Beer has suggested,⁴ or, if haste is imperative, over a roll of gauze on each side, brought out through the wound.

Mention was made of the injection intravenously of blood found free in the abdominal cavity. In a case such as this, or one of ectopic pregnancy, where there has been a sudden loss of a large amount of blood, it has become common practice to attempt to replace the blood into the circulation, either after citration or after simple filtration to remove the large clots. Several instances have recently been reported in the literature, however, where this procedure seemed to contribute to the fatal outcome of the case. It may well be asked whether the blood, which has undoubtedly been changed by its admixture with peritoneal fluid, is to be looked upon as entirely innocuous. It has been shown that blood and pigment injected into the peritoneal cavity can be demonstrated in the lymphatics within as short a period as fifteen minutes. And only recently, based on this absorptive power of the peritoneum, it has been proposed that in small marantic children, in whom intravenous injections are difficult, the transfusion be carried out by means of intraperitoneal injections. We venture, therefore, to suggest that the fluid loss might be replaced by saline infusions and the blood found free in the abdomen be left for absorption by the peritoneum after removing the clots. This procedure would meet the immediate emergency of the hemorrhage without exposing the patient to the added risk, however problematical, of reinjecting a foreign fluid intravenously. Where drainage is instituted, however, it would have certain obvious objections.

(3) PISTOL-SHOT WOUND OF COLON AND KIDNEY

Alfred M., aged twenty-one, was brought to the hospital May 7, 1925, soon after he had been shot with a revolver. There was a wound of entrance in the left hypochondrium, close to the costal border, and a smaller exit wound in the left loin, which region was tender. This sign and, especially, blood in the catheterized bladder urine showed that the kidney had been injured by the bullet. The man was in good condition; his pulse-rate was 96; there were only slight shock and but little abdominal wall resistance.

In the operating-room probing the entrance wound appeared to indicate that the bullet travelled in the parietes without penetrating the belly. The track was nevertheless laid open and thus found to lead into the abdominal cavity. This small hole and the track itself were then closed by sutures; and the belly was opened by a more conveniently placed left rectus-splitting incision. It was then found that the omentum had been torn away from a part of its attachment to the stomach, and that the transverse colon was perforated close to its mesentery and near the splenic flexure. These injuries were repaired by sutures after wiping away the small amount of blood and fæces that had escaped. In the left colonic gutter a large hematoma was seen lying behind the peritoneum. A narrow rubberdam drain was placed in the abdomen, the wound of exploration was closed, and the patient was then placed on his right side. Through a lumbar incision the hematoma was evacuated and the left kidney, still bleeding moderately, was exposed to palpation and inspection. The parenchyma was found completely bisected by a transverse tear across its middle. This was tamponned with gauze packs, and the lumbar wound was otherwise closed with layer sutures.

A few hours later the temperature rose to 105°, as it often does after such a kidney operation, but thereafter the patient made an excellent convalescence. This was marred only by the development of a slough of the aponeurosis in the abdominal wound. When this was extruded, healing took place rapidly and without any apparent weakness beneath the scar.

No escape of urine was noted in the lumbar dressings. The gauze packs were shortened on the seventh and removed on the eighth day. There was then a slight discharge of fluid but it did not have a urinous odor; and 5 grains of methylene blue administered by mouth produced no staining in the wound. The latter healed normally. Meanwhile the patient passed abundant urine, slightly cloudy but containing only a few pus-cells and occasional hyaline and granular casts.

Cystoscopy, May 30th, showed normal bladder appearances, and a free flow of urine was secured on both sides by ureter catheters. The two specimens were practically the same in appearance and in chemical and microscopical characteristics. That from the right side showed rather more (though few) pus-cells than that from the affected side. From the latter, however, *B. coli* was cultured. Fifteen c.c. of sodium iodide solution were then injected into the left ureter for pyelography. This showed some dilatation of the ureter at the crest of the ilium and again near its junction with the kidney pelvis. The latter was normal in size and, except for slight deformity of some of the calyces, normal in appearance.

On June 13th, the patient was discharged in excellent condition, his bisected kidney restored and functioning well.

This case was selected for presentation here because it well illustrates two important considerations in traumatic surgery. The first of these is that stab, gun-shot and other penetrating wounds of the abdominal wall should not be accepted as having failed to enter the belly on the result of mere probing; and if probed at all this should be done on the operating table. *Such wounds should be laid open.* If there is then found an opening into the abdominal cavity the latter should be at once explored through a sufficiently free incision, despite

the absence of shock or local symptoms. As contrasted with spontaneous rupture of an ulcer, traumatic perforation of stomach or intestine with little bleeding is apt to give no symptoms until the leakage assumes threatening proportions. And, too, in abdominal injuries there may rather suddenly develop symptoms of collapse from slow loss of blood by a small vessel, or from a fresh accession of bleeding.

The second consideration is based on observations so often made that it amounts almost to a surgical dictum, *viz.*, that kidney traumata should be treated conservatively, if possible. Even extensive tears, as in this case, have a tendency to heal well, the organ continuing to function. The rule should be, therefore, to stop the bleeding by tampons or by sutures or by both, and, except in the small percentage of cases in which such measures are ineffectual, to let the question of nephrectomy wait on further developments.

(4) TRAUMATIC SYNOVITIS OF THE KNEE—ASPIRATION TREATMENT

Traumatic synovitis, especially of the knee, and whether produced by external violence or by "sprain," is so common in general practice that we have selected some cases to illustrate the treatment we employ routinely on our service.

James H., aged twenty-eight, was admitted September 15, 1925, after his right knee was squeezed between two trucks. The joint was painful and was moderately distended with fluid. There was no discoverable sign of fracture, and röntgenography (routine in all our cases of traumatic synovitis) showed no crack in the bone. The joint was at once aspirated—about 7 c.c. of bloody fluid being thus withdrawn; and a gauze roll was bandaged about it fairly snugly. The patient was instructed to move the joint as much as he could in this dressing, but he was not allowed to walk on that leg. After three days there was no sign of re-effusion and the compressive dressing was discarded. On the seventh day the man was allowed to walk about the ward, on the eighth day to walk upstairs—both without pain or recurrence of swelling—and on the ninth day he was discharged apparently cured.

As Metcalfe⁵ observed in over 300 knee-joint aspirations, and as we have also found and elsewhere recorded,^{6,7} the fluid in cases of traumatic synovitis is, at first, blood or bloody, *i.e.*, the condition is at the outset a hemarthrosis. Gradually, as the blood is absorbed, the fluid becomes pink, then yellow and only after a variable number of days is it "water on the knee."

Because of the constant presence of blood in these joint effusions one must assume, as the gross lesion, that there is a tear in the capsule

and some injury to ligament, cartilage or bone. If an acutely traumatized joint be opened shortly after the injury, the synovial membrane will be found soft, red and swollen, with small fibrin shreds adhering to its surface and floating in the bloody synovial fluid. The subsynovial vessels are dilated and congested and there is an apparent new formation of capillaries. The synovial villi are hypertrophied and congested. Microscopically, the synovial membrane is seen to be infiltrated by numerous small, round and polymorphonuclear leukocytes. There is some proliferation of the fixed tissue-cells and of the endothelial lining of the joint. The fluid in the joint space contains a large number of mononuclear leukocytes which are apparently actively engaged in phagocytizing the red blood-cells. Seen several days later, the fluid has become much lighter in color and the synovial tissue is found to contain a large number of erythrocytes which have permeated the endothelium. The synovial villi are bound together by fibrinous adhesions which are beginning to organize and over which endothelium has already begun to proliferate. If left to itself the fluid is slowly resorbed, but the capsule may remain lax and the intra-articular fat pads hypertrophied and thickened. The presence of fibrin in the synovial fluid, the formation, perhaps, of synovial adhesions and the usual method of treatment of immobilization encourage the occasional development of joint-mice and of joint stiffness.

The generally employed treatment by splinting, strapping, massage, baking, etc., is not only very tedious but also thus quite often leaves a weakened joint. By contrast, aspiration of the fluid promptly relieves pain, restores contour and permits normal motion, and it reduces the period of disability from about eight weeks or more to about two weeks or less.

Aspiration of the knee-joint, especially, is very easy of performance. It is simpler and less hazardous than aspiration of the chest. Under aseptic precautions the chance of infection is very remote. None of the few authors who record experiences with this treatment has noted a single instance of infection. With a stout needle (about 19 gauge), attached to a suitable syringe, the joint or the quadriceps bursa is entered on either side, and as much of the fluid as possible is drawn out, with the assistance, if need be, of compressive manipulation. If, in a few days, the joint refills, the aspiration is repeated.

It is seldom necessary to do it more than twice in uncomplicated cases, unless the patient has borne weight on that joint.

We encourage frequent motion of the articulation immediately after aspiration, but we usually interdict weight-bearing for several days. The patient may walk with crutches, however, putting no weight on the joint. At the end of about a week, if there is practically no effusion, weight-bearing is tried, to be abandoned immediately, however, if there is a recurrence of swelling. Willems, who may be regarded as the father of the aspiration treatment, though not the first to use it, observed that "the goal to be reached is to restore the physiological function of the articulation as much as possible and in the case of the knee, this function is walking." Our own experience and a critical study of that of others demonstrate that immediate weight-bearing causes fresh bleeding, increases the number of aspirations needed and delays the cure.

Benjamin L., a robust man of thirty-one, was admitted November 29, 1924, within an hour after his right knee had been caught between two heavy rolls of paper. There were noted: A slight laceration of the leg near the joint; tenderness over both condyles of the tibia; and a considerable effusion into the joint and quadriceps bursa. Forty c.c. of blood were withdrawn by aspiration, and the joint was bandaged over cotton wool. Röntgenograms showed no bone injury. Bleeding and coagulation times normal. On December 3rd the bandage was removed and the patient moved the knee freely. There was, however, some reaccumulation, and 15 c.c. of blood were aspirated. On December 7th (ninth day) he was allowed to walk. The next day the joint was found again much distended, 60 c.c. of blood were evacuated, and the man was put back to bed for one week. On December 15th he was again allowed to walk. On December 18th: No reaccumulation of fluid; no pain or discomfort; discharged, well.

Bernard G., aged twenty-seven, was seen two days after he had received a severe sprain of the ankle at camp. The joint was much swollen but röntgenograms showed no signs of fracture. About 7 c.c. of bloody fluid were obtained by aspiration. Since the patient found it essential to continue at his work we permitted him to return to his position after applying a Gibney ankle strapping. Two days later, despite the fact that he had been on his feet much of the time, he reported without any signs of fluid in the joint. The strapping was continued for another week and at the end of that time the patient was discharged. Seen several months later, his ankle was quite normal.

In most cases of "sprained ankle" the swelling is not due to effusion in the joint itself and they do not often lend themselves to aspiration as did this case. The ankle is a mortise joint, not subject to the same lateral strain and torsion as the knee; therefore immediate weight-bearing is less apt to do damage. Even in the knee,

especially in mild cases, the surgeon may consent to immediate weight-bearing, *under observation*; but we counsel against it as a routine for we are satisfied from observation that the quickest cure of traumatic synovitis of the knee is accomplished if the joint is emptied by aspiration and spared from supporting weight for a few days.

(5) TORN INTERNAL SEMILUNAR CARTILAGE OF THE KNEE

Dunbar L., aged thirty-one, consulted one of us on September 17, 1925, with his left knee somewhat swollen, painful, and locked in slight flexion. In 1905 he had struck this knee against a fire hydrant, with resulting pain, swelling and inability to walk. After the usual treatment by cold applications, rest, etc., the symptoms subsided and he remained well until 1923 when his knee "slipped out of joint" while he was bowling. He "set it in place" but the joint felt weak and the symptom recurred frequently, especially while playing tennis. It happened four times in the nine days preceding his visit. The day before this consultation, while bending forward, he felt a snap in the knee and the leg gave way. He was unable to reduce the dislocation of the cartilage this time and could not extend his leg beyond 160°. Some crepitus could be demonstrated on the inner aspect of the joint. By manipulation—flexion, internal rotation and extension—reduction, probably imperfect, was secured, and the extended joint was strapped and snugly bandaged. The next day there was a repetition of the "dislocation" and the locking. The patient was then sent to the hospital. Pneumoröntgenography of the joint, as developed by Kleinberg,⁸ was not resorted to, for the diagnosis was quite evident.

Arthrotomy, September 19th, showed a torn and curled internal meniscus, a swollen and congested post-patellar fat pad, and an hypertrophied synovial tag. This tag and all but a small, well-attached posterior portion of the meniscus were removed. The joint was closed in layers with plain catgut and bandaged in a gauze roll, without a splint. After forty-eight hours, active motion was permitted, in bed. Three times post-operatively the joint was aspirated because of reaccumulating effusion. Healed *per primam*, the patient was allowed out of bed on the ninth day, but weight-bearing was interdicted. On the eleventh day walking was instituted, but the reappearance of fluid caused the patient to be put back to bed for another week. Thereafter, on walking, the reaction was very mild and he was discharged with a slight swelling, but with a normal range of free, painless motion. Examined a month later, the joint was found strong and of normal contour, the patient walked without pain or fatigue and had full range of motion.

We pass over, as familiar, the symptomatology, conservative treatment and operative indications of dislocated internal meniscus, and present this case to discuss certain details of surgical technic and post-operative management.

The arthrotomy was performed with a tourniquet applied to the thigh after emptying the blood-vessels of the extremity with a Martin

bandage. The leg hung over the foot of the table, the knee thus flexed to a right angle (Jones' position). We also followed Jones in cutting into the joint through a piece of wet linen (or gauze) fastened smoothly around it, and in using a strictly "no-touch" technic throughout the entire operation.

We might also have used the slightly curved incision of Jones⁹ which "extends from an inch within the lower angle of the patella to half an inch below the tibial margin, curving more acutely at this point toward the lateral ligament." We employed, instead, the also slightly curved and higher placed incision described by Fisher¹⁰ because it seems to us to give a somewhat better exposure of the internal (or, as the case may be, the external) compartment of the joint. The lateral ligament must not be cut, of course. Roberts¹¹ has described a clever approach to the cartilage through a V-shaped cutaneo-periosteal flap, chiefly over the upper end of the tibia, the lower surface of the meniscus appearing on the under surface of the flap; and he recommends it as permitting early flexion to 90° without strain on the wound. It seems to us to have the great disadvantage that it does not give sufficient exposure of the joint to discover associated lesions. Such exposure is important, as is illustrated in this case, in which an hypertrophied synovial fringe was found and removed. A piece of articular cartilage loosened from the femur or patella will not be discovered röntgenographically unless it bears a fragment of bone. Indeed, in cases in which the diagnosis of loosened meniscus is at all in doubt it is better to expose the entire joint freely by the split-patella arthrotomy of Jones⁹ or by one of the patella-dislocating approaches, such as that of Fisher.¹⁰

We do not follow Jones in splinting the knee for twenty days, but encourage early, active (not passive) motion of the joint. Whipple¹² showed in a parallel series of cases, immobilized and mobilized, after arthrotomy for displaced meniscus and for loose bodies, that those treated by early active motion had a shorter stay in hospital and an earlier return to optimum anatomic, symptomatic and economic result. We are not quite satisfied, however, that it is desirable to start motion as soon as the patient recovers from the anæsthetic, as Whipple, Roberts and others recommend. It will still be early enough, it seems to us, if this be delayed a day, or two days, until the likelihood of starting fresh bleeding is passed.

After an arthrotomy the joint fills with fluid—bloody fluid. This we treat, as we do traumatic synovitis, by aspiration, repeated as often as necessary. In this case it was done three times. Also as in traumatic synovitis, though the patient may soon be allowed out of bed, we forbid weight-bearing as long as there is any tendency to joint swelling, and we discontinue weight-bearing if it produces more than a slight re-effusion.

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Progress of Medicine

for 1925*

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INTRODUCTORY REMARKS

"On the one hand, medicine is increasing its contact with the sciences, and, on the other hand, is extending the range of its influence to cognate activities in the body politic. Medicine has, so to speak, an outer and an inner temple. In the inner temple thought reigns, and in the outer action becomes the handmaid of thought."

LORD DAWSON OF PENN.^{39/1-2-1926}

THE science of medicine is advancing by leaps and bounds, leaving its older companion, the art of medicine, lagging sadly behind. Thus, a negative skiagraph (Fig. 1) was recently sent over a telephone wire from New York to Chicago in seven minutes, and the positive print (Fig. 2) was returned by aeroplane to New York for publication the following morning in one of the newspapers there. Again, milk and olive oil exposed to ultra-violet light have been shown in the treatment of rickets to possess the therapeutic value of cod-liver oil and of the light itself. Notwithstanding these wonderful new aids to medicine, back to physical diagnosis and the treatment of the individual

* The first arabic number above a proper name or disease, and at the end of a paragraph is the key to the journal named in the list of medical references printed at the close of this article from which the reference, thought or abstract is taken; the next numbers refer to the month, day of the month in which the journal was published, while the year of *those references published in 1925*, the period more especially covered by this article, is not given. All references in which the year is not mentioned, therefore, appeared during 1925. In those instances where apparent omissions of important medical matters are noted, the reason will usually be found that original papers covering the subject have already appeared in the pages of the INTERNATIONAL CLINICS during the past several years or articles are in course of preparation for future publication. Mrs. Mildred K. Smith, of New York City, has furnished the abstracts from articles selected by us for editorial revision of about one-half of the subject-matter here presented, for which we extend our thanks.

FIG. 1.



Reproduction of original X-ray negative of hand, with ring on finger. (Courtesy of *Radiology* and the General Electric Company.)

FIG. 2.



Positive print from unretouched negative as received by telephone wire in Chicago from New York. (Courtesy of *Radiology* and the General Electric Company.)

patient rather than the disease from which he is suffering, continued to gain ground during the past year, while the reaction against too much dependence upon laboratory methods *per se* continues. Not that there has been any diminution in the use of such tests, but there appears to be by those clinicians who are keeping up with the times, a more proper interpretation of their advantages and limitations and cost of time and money in proportion to their real value.

That grand old master of medicine, Sir Thomas Clifford Allbutt, died on February 22, 1925, after eighty-eight years of a strenuous and useful life. From his writings and those of Osler alone could easily be reproduced the real progress of internal medicine for the past sixty years, well-illustrating the value of the old teaching institutions of Cambridge and Oxford. Colonel Fielding H. Garrison ^{57/III-27} in an appreciative obituary quotes Allbutt as having written over thirty-five years ago:

"Gout and cancer are autogenous, smallpox and ague extraneous in origin; in phthisis, the extraneous cause is a touchstone of diathesis. All diseases of modern peoples become neurotic in type, as Cullen surmised. Changes in types of disease are due to this fact and to the racial (*i.e.*, chemical or metabolic) complexion of peoples. Diseases must be studied in family trees. There are even pathological races of people, set off by atavism. Each disease is only a member or term of a series—*e.g.*, the rheumatic series (purpura, urticaria, pemphigus, erythema, endocarditis, chorea, arthritis), or the gouty series (dyspepsia, arthritis, phlebitis, arteritis, nephritis, angina pectoris, migraine, hypochondria, insanity, eczema, glycosuria, neuritis, bronchitis, tonsillitis, hæmorrhoids, purpura). Fever is a thermo-ataxia. Gout implies the metabolism of a bird. Infection and immunity are analogues of impregnation and sterility in sexual congress. Each locality or race has diseases peculiar to it. Each tropical country has its own kind of tropical medicine. Malarial fever in a locality usually connotes infrequency of cancer, typhoid, phthisis, insanity (neurosyphilis) and epilepsy. Poisons of active principle (acid) type produce hyperthermy, poisons of alkaloidal (basic) type hypothermy. Curare turns a mammal into a cold blooded animal. Poisoning and detoxication turn upon isomerisms and molecular vibrations."

A new combination of a number of minor advances in medicine, running over a period of years, often produces a happy result which is even more striking in the saving of human life or the relief of suffering than is a single new, but important, discovery. Dr. William J. Mayo ^{15/XII} in an address delivered before the section on surgery of the Medical Society of the State of Pennsylvania, Harrisburg Session, October 8, 1925, cited four case histories which we reproduce complete, showing conclusively true progress in medicine of the right sort.

"SILENT" DIABETES

CASE I.—The patient, a woman aged forty-four, had had malignant disease of both ovaries and tubes, for which abdominal hysterectomy was performed. She left the operating table in good condition, but six hours later developed coma, no clue to which had been given in the history or preliminary physical examination. Examination of the blood showed a very low sugar content. An intravenous injection of 10 per cent. glucose solution with bicarbonate of soda and a moderate amount of insulin were given. The patient regained consciousness in a few moments. Intravenous injections were continued for three days, and convalescence was rapid. The patient left the hospital in due time, and has remained well.

Comment by Doctor Mayo.—Wilder and Adams have recently reported a series of 141 cases in which major operations were performed for general surgical conditions, complicated by diabetes, with but four deaths. Many of the patients had severe diabetes, and all of them recovered.

ALKALOSIS

CASE II.—The patient, a man aged thirty-four, had a large, anteroposterior bleeding duodenal ulcer with moderate obstruction. The ulcer was removed by direct excision, and a partial duodenectomy made. The end of the stomach was attached to the cut end of the duodenum after the general plan of the Billroth I pylorotomy. At the end of four or five days the patient began to vomit. Large quantities of fluids were removed from the stomach by tube, and sustenance was maintained by proctoclysis and hypodermoclysis. In the course of three days symptoms of tetany appeared, and his condition became serious. Examination of the blood showed the chlorides to be reduced to about half the normal of from 560 mg. to 650 mg. The alkalosis was even more clearly demonstrated by the carbon dioxide combining power rising from the normal of 56 to 65 per cent. by volume to 140. The urea blood content had risen to 125 mg., and the creatinin to 10 mg. The patient was given a litre of 1 per cent. sodium chloride solution with 10 per cent. glucose intravenously three times in each twenty-four hours. He began to improve at once. The chloride rose to normal, the dehydration was relieved, and the renal function became adequate, the blood-urea dropping to normal. The patient left the hospital at the end of fourteen days in good condition, and has remained well.

Comment by Doctor Mayo.—Balfour, Eusterman, McVicar, and Weir, with these methods of restoring by biochemical means the vital capacity of patients, have noted remarkable results from operating for surgical conditions of the stomach and duodenum. In a series of over 400 consecutive cases of cancer and ulcer of the stomach and duodenum, Balfour has been able to lower the operative mortality to less than 1 per cent. Of the four deaths which occurred in the series, one followed jejunostomy for an acute perforating gastric ulcer, with

general septic peritonitis. In this series of over 400 cases, resection of the stomach was performed in 114 with but two deaths. A large percentage of the operations were performed for carcinoma, only four were indicated for duodenal ulcer, which is essentially a benign process seldom requiring so radical a procedure, and the remainder for gastric and gastrojejunal ulcer.

JAUNDICE

CASE III.—The patient, a woman aged forty-eight, came for examination in poor general condition, with jaundice of ten weeks' duration. She gave a clear history of gall-stone colic over many years. For the last five years she had had comparatively little trouble from the gall-stones. Otherwise she had been in good health. About four months before coming to the Clinic her appetite had failed, and she had lost considerable weight. Jaundice had slowly developed and had been continuous. There had been times when she had a chilly sensation, but no record had been kept of her temperature. Besides the jaundice, there was a tumefaction in the region of the gall-bladder which was believed to be distention of the gall-bladder, and possibly a complicating carcinoma. Except for the presence of bile in the urine, the renal function was fair. The stools were clay-colored. The skin showed some bluish discolorations as the result of slight injuries, and evidences of irritation from scratching to relieve the intolerable itching which accompanied the jaundice. The coagulation time of the blood was 22 minutes; the calcium time was 20 minutes. Calcium chloride was given intravenously, blood was transfused, large amounts of water were introduced to aid elimination, and diet with considerable carbohydrate was prescribed. In the course of a week the coagulation time of the blood was reduced to nine minutes, and the patient's condition greatly improved. Exploration under local anæsthesia, aided by a small amount of ethylene and oxygen, revealed stones in the gall-bladder, and a small obstructing malignant mass in the terminal end of the common duct. The stones were removed from the gall-bladder, which contained only white bile. The gall-bladder was anastomosed to the stomach and the abdominal incision closed. The patient did badly following operation, was unable to take nourishment, became more dehydrated, and developed diarrhœa, the stools showing evidence of bile. The output of urine was greatly reduced. She became somnolent, and gave every indication of speedy dissolution. Examination of the blood showed acidosis. The carbon dioxide combining power dropped from the normal of 56 to 65 per cent. by volume to about 20 per cent. The patient was given a litre of glucose and bicarbonate of soda solution intravenously three times a day, and began to improve immediately. She left the hospital in four weeks, and lived in comparative comfort for about nine months. Necropsy showed malignant disease of the ducts with secondary involvement.

Comment by Doctor Mayo.—Walters, by careful rehabilitation of jaundiced patients, has been able to reduce the operative mortality to 3 per cent., and to bring to operation safely many patients of the type formerly considered beyond help.

URÆMIA

CASE IV.—An anæmic man, aged seventy-six, came for examination because of urinary frequency, dizziness, and slight edema of the ankles. In the lower abdomen was a mass which was recognized as the distended urinary bladder. The blood-urea content was 300 mg., the creatinin 8. The urine contained considerable albumin and casts. The prostate was markedly hypertrophied. The history and physical findings were typical of prostatic hypertrophy, with secondary involvement of the kidneys, and marked urinary retention. The patient was placed in bed, and the bladder slowly decompressed. Eventually, tolerance to the inlying catheter was established. A large amount of fluid was given by mouth, and from 1000 to 2000 c.c. of a 1 per cent. sodium chloride solution intravenously each day. The patient was given two small transfusions of blood, and placed on an easily digested carbohydrate diet. In two weeks the urea and creatinin had dropped to normal, and his condition was favorable for operation. Suprapubic prostatectomy was performed. Recovery was prompt, and the patient left the hospital in good condition, which he has maintained.

Comment by Doctor Mayo.—Braasch, Bumpus, Hunt, and Walters, by careful preparation for operation and proper after-care, based on these conditions, of patients with prostatic hypertrophy, have been able, since January 1, 1925, to perform prostatectomy in a series of 186 consecutive cases, with but one death.

TRAINING OF PHYSICIANS AND NURSES

An adequate number of properly trained physicians and nurses to give the population at large proper medical attention, is a problem which has received much consideration during the past year, owing to the fact that the rural population is not sufficiently supplied with physicians and the cities with nurses. The Philadelphia County Medical Society on December 9, 1925, devoted an entire evening to the subject of medical education. Dr. William Allen Pusey, an ex-president of the American Medical Association, told of what had been done in the past twenty years in increasing the requirement in medical education. He then stated: "It is probably within the facts to say that the average age of the doctors in rural districts of the United States is at least fifty-two years. In some states it seems to be as high as fifty-six or fifty-seven. That, of course, means that the country doctor is disappearing. . . . The seven-year doctors we are turning out are nearly all coming from the city because the city boys are the only boys, who want to study medicine, who can afford to do so, and they are staying in the city to practise, nearly all of them as specialists. . . . If we are going to get students to do the ordinary work

of the world, either in the city or the country, we have got to put medical education in its demand on an equality with other learned professions. That would mean a minimum requirement of four years after leaving high school." 61/xii-19

The United States Army has adopted its own method for filling the ranks of the Medical Corps now that the best of those studying medicine are attending the R.O.T.C. camps during the summer. A competitive examination of those graduating in 1926 was held for filling internships in army hospitals, providing the one passing the examination was later on found to be physically fit. Upon graduation they will receive commissions as First Lieutenants in the Army Medical Reserves, receiving the pay and allowances for this grade, and will begin active service as interns August 1, 1926. If at the end of one year they receive favorable recommendation from their commanding officers they will be eligible to appointment for the regular medical corps without further examination, other than physical. The first sixty names from twenty-three medical schools have just been announced.

Turning to the nurses an editorial in the February 6, 1926, issue of the *New York Medical Week*, official organ of the Medical Society of the County of New York, we read:

"With the passage of an enabling resolution by Queens, the county medical societies of the Greater City can now proceed with the work necessary to carry into effect the plan devised by the Medical Society of the County of New York to overcome the existing shortage of nurses. Discussion of the proposition now under way has elicited the fact that physicians throughout the city believe the inadequacy of the present supply of nurses to be due, in part, to the stress laid by the State Nursing Board upon unimportant domiciliary details, in part to the elaborate theoretical structure that has been reared about nurse training. It is true that there are other factors contributing to the insufficiency of the annual number of graduates, but these are the two principal causes. In nursing circles there has been a great deal of misunderstanding on the score of what the doctors plan. It is rumored that the medical societies seek to force the nurses into mean living quarters, to compel them to work long hours for poor pay. Those who are responsible for these rumors are misrepresenting the facts. The medical profession concedes as a matter of course the right of the nurses to decent working conditions and such compensation as will enable them to maintain a proper standard of living. It is our belief, however, that the appropriate city department, and not the State Nursing Board, should set the criteria for the housing of nurses as of every other student and working group. The tendency of the day would guarantee the comfort of the quarters once they were pronounced hygienically suitable. It seems incontestable that since the nurse is the doctor's

assistant, he should be allowed to set the requirements which will produce the type of aide he needs. Under the jurisdiction of the State Board, the present-day nurse frequently brings to the physician a host of highly theoretical principles for which he has no use, and a dearth of the practical lore and bedside presence he requires. The nurse cannot go her own untrammelled way without regard to the qualities that the doctor wants in her, any more than the stenographer or bookkeeper can pursue a course of training incompatible with the duties her employer expects her to perform. Believing that it is the State Board, and not the individual nurse, who is responsible for the troublesome situation existing to-day, the organized physicians of the city have united to set their own standards for training schools, regardless of the powers at Albany. Now that Queens has fallen in line, work can begin."

CANCER

A careful analysis of the literature on cancer research for the year—given later on in detail under cancer in its alphabetical place—indicates two important advances, first that the nutritional study of both tissue and new-growth cultures is offering considerable promise of valuable information in this subject. Alteration in the amount of food and oxygen, especially a decrease of these, as produced by the repeated processes of abortive repair consequent upon repeated low-grade types of chronic irritation, have been found as a fairly constant factor in the causes of new growths, by many investigators approaching the subject from several different angles. The influences of a virus, of a tissue extract, or of an enzyme, have been advanced by different workers as a cause of new growth or as a factor necessary to their continued cell-division and extension. From the standpoint of nutrition, fat has occupied an important position, as the fat solvent agents have been shown to have an influence upon the production of cancer by their ability to divert to themselves the fats within the cells in this process. Though there is a very large group of investigators who favor the parasitic theory of cancer, the definite proof of these agents as furnishing anything except the irritating factor is scouted by many pathologists. Michael Levine, in the *Journal of Cancer Research*, claims that the so-called "cancers" of plants differ markedly from true cancers, resembling them only as any rapidly growing tissue does. The important gains made in this subject will serve to narrow somewhat the broad collateral character of work made necessary by any institution making a study of this condition, allowing most of the research to be concentrated on the physiology, the chemistry, and the cytology of cultures of these tissues.

Alexis Carrel ^{35/vi-13} cites an early experiment where blood macrophages were rendered malignant *in vitro* by the action of the filtered extract from the Rous sarcoma and these cells in turn produced the Rous substance and died. The process is compared in its action and in its appearance in the cultures with the production of a bacteriophage, as observed by Twort and d'Herelle. The same phenomena were produced by using the McFaul tar sarcoma, and the conclusions drawn are that this principle is common to all sarcomas, that tar sarcoma appears to be a self-perpetuating alteration of the metabolism of embryonic cells produced by the action of coal-tar, and that certain substances produced by bacteria, by helminths, by the action of X-ray, produce in macrophages and other cells a defect which reproduces itself. By a similar method the toxins normally found in the adult blood stream may spontaneously produce new growths.

ROCKY MOUNTAIN SPOTTED FEVER

The United States Public Health Service believes that it has produced a vaccine which may protect human beings against "tick fever," which occurs principally in certain northwestern states. One of the officers of the Public Health Service, Assistant Surgeon McClintic, contracted Rocky Mountain spotted fever while engaged in experimental studies in Montana and died in line of duty as did also the Laboratory Assistants William E. Gettinger and George Cowan, thus adding three more names to the long list of those who have sacrificed themselves to the good of science.

MISCELLANEOUS TOPICS

Science Service of Washington reports *inter alia* the discovery by Robert C. Green, of the University of Minnesota, of the causative agent of distemper in dogs; that Dr. A. Besredka, of the Paris Pasteur Institute, has found that deadly germs may be made harmless by cultivating them on tissues on which they are not accustomed to prey; that foot-and-mouth disease of cattle was controlled in Denmark with serum treatment instead of slaughtering herds; that certain soil bacteria act on plants like vitamins do on animal growth; that vitamin E, necessary for reproduction of offspring, is found in many vegetable and animal substances; and that Yale University has a new method of measuring the flow of blood quantitatively.

ANÆSTHESIA

Preliminary Injections of Morphine and Magnesium Sulphate.—J. T. Gwathmey^{35/x1-7} shows that a synergism exists between magnesium sulphate, morphine, and ether, which, if administered together in an anæsthesia, reduces the dose of ether necessary to produce narcosis to one-half, decreases the post-operative nausea, vomiting, and pain to a marked degree and thereby decreases the dangers of general anæsthesia and its complications to a minimum. Quoting several other workers, and citing experiments on animals and in clinical records these authors conclude that the addition of 2 c.c. of a 50 per cent. solution of magnesium to a hypodermic of morphine increases its physiological effect from 50 to 100 per cent. The combining of these two drugs does more than increase the action of the morphine and prolong its effect, it maintains the respiratory rate at normal, shortens the induction time, decreases the amount of ether, and the resulting shock consequent on it, and makes the whole process a less stormy procedure. Post-operative nausea and vomiting are reduced and are often completely absent, and wound and gas pains are reduced so that convalescence is smoother and more rapid. Experiments on animals show that the amount of ether necessary to produce narcosis is halved and its lethal effect is likewise cut in two. Procaine 2.5 per cent. was added to the hypodermic solution of morphine and magnesium sulphate.

ANAPHYLAXIS See **ASTHMA**

ASTHMA

In a preliminary report, George L. Waldbott^{12/x1} points to experimental work which suggests that there is a definite relationship of the lymphatic system, of which the spleen is a part, to anaphylaxis. It would seem also that the removal of the spleen reduces the power of an animal to produce antibodies, while irradiation of the spleen seems to increase the antibody titre of the blood. On the basis of these findings, Waldbott undertook clinical studies on a small number of asthma patients. Under röntgen-ray treatment of the spleen most of these patients improved, while in one case the results were striking. A boy aged six and a half years, who gave positive skin tests to milk, casein, whole egg and wheat, received one röntgen-ray treatment of the spleen. The dose consisted of 5 ma., six minutes, 4 mm. aluminum, 88 kilowatts, 10-in. skin target distance. In addition an anti-anaphy-

lactic diet was instituted for two weeks. The result was entire relief from clinical manifestations for a period of eight months. Following the röntgen-ray treatment the blood-calcium rose slightly, the eosinophile count decreased and the skin tests became negative. Two German writers, M. Groedel and H. Lossen, analyze 71 cases of bronchial asthma in which the spleen was irradiated. In 10 of these cases the results were questionable; in 7, negative; in 15, good; in 12, very good, and in 27, splendid.

Treatment of Asthma.—W. L. Brown ^{19/vii-29} sums up the present knowledge of asthma from the standpoint of its cause and mechanics, with a view to its logical therapeutics. He defines this disease as an unstable or irritable condition of the bronchomotor and vasomotor portions of the nucleus of the vagus nerve, which causes it to react explosively to psychical and peripheral stimuli, and to foreign proteins, producing bronchomotor spasm, and vasomotor turgescence. He infers that psychotherapy, protein sensitization, and the treatments aimed at vagotonia and endocrine imbalance, are not sufficient in handling these conditions. Asthma often occurs in neuropathic families, and the production of paroxysms by an artificial flower illustrates the importance of the psychic factor in this disease. The defense reaction of one individual when exposed to a psychic conflict may produce a hysterical paralysis, while these patients develop asthma under the same stresses. The peripheral stimuli which can act as the exciting cause of this process are very numerous and the author cites eye-strain, hay fever, nasal disorders, sinus infection, enlarged bronchial glands, and healed tuberculosis. Immunity to foreign proteins consists of the ability to assimilate them, and thus build them up into the specific proteins of the body. Man is naturally immune to some foreign proteins, and acquires through inheritance or other means the immunity to others. Practically everyone has sensitivity to some of these substances, and the asthmatic is the individual who has failed to develop this faculty or loses it through some disease process. There is no limit to the variety of these proteins to which man may be sensitive, and they range from all kinds of food to emanations from animals, bacteria, pollens and drugs to include almost any animal or vegetable substance that can be ingested or inhaled. The parasympathetic system controls this process, and decides whether a substance ingested is to be assimilated or

rejected, similarly when material is inhaled the production of a cough or a bronchial catarrh is the process by which it is eliminated. Bronchomotor spasm is a violent action of the surface tension, of the enormous area of the respiratory tract in an effort to contract and expel the irritating substances. The sympathetic and the endocrine systems are the balancing antagonists in this process, and part of the defensive function depends on their ability to increase the blood-sugar and its adrenal content. The value of this extract in treating anaphylactic shock, and the influence that fatigue has in precipitating this condition have led many investigators to believe that the substances which are able to produce asthma depress adrenal function. The thyroid, the posterior portion of the pituitary, and the adrenals coöperate with the sympathetic in the defense against this reaction and are valuable in its treatment. The fact that the paroxysms come on very often during sleep, when the sympathetic has the upper hand, is additional proof of this theory. Likewise any defect of the whole chain of the endocrine system may, by upsetting the defenders of this barrier, and uterine disease, or other lesions of the gonads, play a part in this process. The eczemas are an attempt on the part of the skin to assist in the excretion of these toxic substances, and it is thought that the rashes of the infectious diseases represent a severe anaphylaxis at the negative phase in the curve of antitoxin production, and is probably the sign that determines that the infection has defeated the defense processes. The rôle of the eosinophile in asthma, in urticaria, and in intestinal infections, especially those of the nature of food poisoning, is significant evidence for these relations. The value of desensitizing the patient to the substance, which acts as the exciting cause, is fairly well established, but the treatment of the endocrines aimed at restoring any imbalance, the removal of mechanical excitants in the respiratory tract, the removal of infectious foci, and similar general adjunct treatment is necessary. Adrenalin, thyroid extract, iodine probably because of its effect on the thyroid, pituitrin, atropine because of its effect on the parasympathetic endings, peptone, arsenic and oxygen, are all valuable.

AVITAMINOSIS

Diagnosis.—B. Leichtentritt ^{44/v.xxix,p.490} finds that keratomalacia and xerosis, alimentary cedema, and scorbutus usually appear in youth, since growing tissue is peculiarly sensitive to nutritional deficiency.

There may be lack of vital elements in food or constitutional lack of ability of cells to utilize food. A connection exists between infection and nourishment; adequate food in all respects being the best guard against infection. Rich vitamin diet shows its effect in counteracting tuberculosis. Infection, again, has an injurious effect upon the healing of avitaminotic conditions. Lack of nourishment is seen in skin and hair disorders, and sensitiveness of skin to cold or heat. There is delay also in healing of wounds, and glandular disturbances result. Avitaminosis causes changes in serum substance. In avitaminotic conditions there is failure of human serum to prepare itself the trypanocide toxin, which can otherwise be produced. If infection enters during avitaminosis, disturbance results, through the interrelation of the reticulo-endothelial system and the immunity processes. In children with alimentary disorder, especially in cedematous condition, and in older persons with alimentary affection, diphtheria bacilli are greatly altered in the serum, appearing themselves cedematous, grain-like, split, and enlarged. This can be produced and cured in experimental animals practically at will.

The condition of avitaminosis due to imperfect assimilation may be called an avitaminotic cellular complex. Avitaminotic growth forms are most closely associated with this. If these are not easily detected, a condition which may be called hypavitaminosis, the bacteria test will reveal the condition. Perhaps many childhood nutritional diseases belong to this condition.

BACTERIOPHAGE

A comparative study of a diastase, and its complement on the bacteriophage, was carried out by Fernand Arlóing, L. Langeron and Sempé.^{24/11} The diastase used was the urease extract of *Soja hispida*. With this diastase the specific action is very rapid (two to five minutes), it is less rapid for the complement (thirty minutes) and slow with the bacteriophage (twelve to twenty hours). The dose of urease necessary to produce the specific reaction is not of importance and it is of slight importance for the bacteriophage; it is quite important, however, for the alexin. Ageing has the effect of rapidly attenuating the reaction on the diastase in the humid state; it is practically without effect on the bacteriophage, while it destroys the complement. Agitation in the free air causes the complementary function of the serum to disappear; it has no effect on the urease and the bacterio-

phage. Heating to 60° destroys the complement in forty-five minutes and the diastase in twenty to twenty-four hours; it has no particular effect on the bacteriophage. Adsorption is easily brought about with the diastase; it is partial with inert powders (kaolin), and complete with a colloidal precipitate (sulphate of aluminum). The same is true of the complement. On the other hand, with these substances, there is practically no adsorption with the bacteriophage, but this is almost completely adsorbed on contact with living cells (red deplasmated and washed sheep cells). Prolonged centrifugation (over sixty minutes) exercised no action on any of the three products studied. Filtration through a Chamberland filter with slight pressure (20 cm. Hg) eliminates the complement in one filtration, and the diastase in three filtrations, while the bacteriophage passes through a porcelain filter indefinitely without being altered. These effects, almost opposite in some instances, serve to differentiate urease, complement and bacteriophage.

BLOOD

Sedimentation Test as an Aid to Diagnosis and Prognosis.—According to Frosch ^{30/x} the usual method of performing the red-cell sedimentation test is by the Linzenmeier technic. Into a 1-cm. tuberculin syringe, which must be absolutely clean and dry, is drawn 0.2 c.c. of sterile sodium citrate of 5 per cent. strength. To this is now added 0.8 c.c. blood drawn directly from the vein, without the use of a tourniquet as the stagnation of the blood increases the relative cell content and the carbonic acid, both of which may change the end-results. The contents of the syringe are thoroughly mixed and emptied into specially made tubes, 6.5 cm. long, 5 mm. in diameter with a capacity of a little over 1 c.c. and marked at 6, 12, 18 and 24 millimetres. The time it takes for the red cells to reach the 18-mm. mark and leave the plasma above it clear, is called the sedimentation time. By agitating the tube the test may be repeated, and should yield identical results. The test was performed by Herman L. Frosch on 100 consecutive cases at the Lebanon Hospital, New York City, and by O. R. Nees ^{60/xii} at the U. S. Naval Hospital, San Diego, California, in about 150 cases. The clinical applications that may be made of the sedimentation test are numerous. In surgery, any patient having a sedimentation time of one-half hour should be operated upon immediately, because this is an indication that the inflammation is very

marked and that waiting is dangerous. In appendicitis before rupture the test is practically normal. In gynæcology, if one believes that a case of salpingitis should not be opened up during the acute stage, then a patient with a sedimentation time of half an hour or less should absolutely not be operated upon. Linzenmeier found in normal pregnancy after the fourth month that the blood settled to the 18-mm. line in three to five hours. If in less than forty minutes some complication, usually of an inflammatory nature, is present. No case of adnexal disease should be operated on, unless sedimentation time indicates that all latent foci of infection have been eliminated. In general medicine the prognosis should be very guarded in a case having a sedimentation time of less than half an hour. The test done at different intervals of the illness will show whether the patient is improving or is getting worse. Briefly, an increasing sedimentation time in a patient means improvement. A diminishing sedimentation time means that your patient is getting worse, even though the clinical picture indicates improvement. The temperature does not in any way seem to affect the sedimentation time. Nees, working with Miller, observed in tuberculosis that the decrease in sedimentation runs strikingly parallel with the clinical improvement of the patient, a rising sedimentation being, therefore, a favorable prognostic sign. Thus, there is no active tuberculosis present in the patient under examination if the sedimentation test is normal, running from four to nine hours, and there would appear to be no clinical significance to a slow sedimentation rate.

BLOOD-PRESSURE

Effects of Hepatic Extract on High Blood-pressure.—A. A. James and N. B. Laughton ^{23/vii} found that in experimental animals extracts of liver effectually reduced hypertension induced by pressor substances such as epinephrin, pituitrin, iso-amylamines, and parahydroxyphenylamine. These extracts will reduce blood-pressure to a low level (about 50 mm. Hg) where it is capable of being maintained over long periods of time. Large doses reduce blood-pressure to its lowest level and death ensues. Livers from the rabbit, dog, beef, calf and pig were employed. At first, simple saline extract was used, but later this was greatly modified. The exact chemical nature of the compound is still unknown. Preliminary experiments suggest that it is not cholin, as it is very much more potent than cholin itself.

Forty-two patients, both bed and outdoor cases, treated by R. H. Major^{35/vii-25} with extract of liver showed an average of 35 mm. Hg fall in blood-pressure above normal; while normal pressures were not changed. The best extract is one fairly free from proteins made by fractional alcoholic extraction. The permanency of this treatment is committed to further experiments.

CANCER

Probably no branch of medical research has commanded so much attention during the year as the cancer problem. Numerous articles have appeared, containing new information along several of the most promising avenues of investigation that have been opened in the last few years. The newspapers have carried notices, of a most startling character, indicating to the general public that the cure of this dread disease was forthcoming. These articles have not been confined to the so-called yellow sheets, but have appeared in the most conservative journals. The first suggestion of these reports was an original article by W. E. Gye in No. 3 of Vol. 2 of the *Lancet* for 1925. This author, working with the Peyton Rous malignant, spindle cell, sarcoma of fowls, known as chicken sarcoma No. 1, which is transmissible through the use of cells (killed by drying, or with 50 per cent. glycerol) as well as with a cell-free Berkefeld filtrate, established the following claims. The first experiment showed that a fairly constant relation exists between the size of the dose of the filtrate, and the size and killing time of the resulting tumors. One c.c. of the filtrate used produced a discernible tumor on the fourteenth day, which killed in four weeks. One-half c.c. produced a larger tumor, which allowed the animal to live thirty-five days, while smaller doses produced delayed tumors which disappeared. The second series of experiments were made to establish the so-called infectivity of the primary cultures. This consisted of incubating 0.5 gm. of the tumor in 5 c.c. of broth anaërobically and aërobically at 37° C. The supernatant fluid remains infective in the aërobic tube for two days, and for four days in the anaërobic one. This is made surer in its difference of action if the entangled air is removed with a Geryk pump. The addition of rabbit serum to these incubation tubes about doubles the time they remain infective in both the aërobic as well as the anaërobic tubes. The author claims to have repeated these experiments often enough to make them conclusive. Peyton Rous had shown that carbolic

acid, toluene and chloroform destroy the agent which transmits this sarcoma. Gye confirms this, and in addition shows by a set of trials that incubation at body temperature enhances the killing power of chloroform upon this agent.

The next set of experiments that were made showed that there are two factors in these cultures, which determine the transmission of this sarcoma by this means. One of these is a labile chemical substance, resistant to chloroform, and the other a virus, which disappears on aërobic incubation at the end of three days. It is apparent from these experiments that a culture freed from this virus by a three-day incubation under aërobic conditions, and that a filtrate treated with chloroform fails to reproduce the tumor, but that combined, these two factors will constantly produce the new growth. The author then conducted a long series of centrifugations of the filtrates from these cultures, and came to the following conclusions: That in the primary cultures, as well as in the candle filtrates of this tumor, there are two factors necessary to transplant the tumor, one having the character of a virus, thrown down in the centrifuge, while the other is uninfluenced by it, and therefore probably a chemical substance. The writer concludes that the chemical substance, which can be separated from the cells of the tumor, is the specific factor, that the virus is non-specific, and can only act in the presence of the chemical one, which determines the cellular character of the tumor. Gye proved the non-specific character of the virus, by freeing Jensen's rat sarcoma, rat carcinoma No. 9, and mouse carcinoma No. 63 of their specific chemical factor, combining their cultures with the specific factor of Rous's tumor, and constantly producing in chickens the typical cellular picture of this sarcoma.

The same characteristics which held for the Rous chicken sarcoma were not proven for Jensen's rat sarcoma, rat carcinoma No. 9, and mouse carcinoma No. 63, in that a cell-free filtrate of these would not produce a tumor. It is not evident from this first report that the specific factor of the other tumors was tried with the non-specific factor from the Rous tumor in the chick, nor that the other possible cross-control experiments were tried with the different tumors and animals concerned.

The last set of experiments consisted of injecting the specific factor of Rous's chicken sarcoma with the cultures of three human

cancers. Two of these became contaminated and were failures, while the third, an adenocarcinoma of the breast, produced tumors in the chicks, both from the primary tumor, and from an invaded axillary lymph-node. These tumors were histologically identical with the original Rous sarcoma. Mouse sarcoma 37/S acted in the same way that the Rous sarcoma did, though the specific factor proved more difficult to concentrate, being less abundant or more labile than the same factor in the chicken sarcoma.

In conclusion, the author feels that new growths are specific diseases, caused by two separate factors, one a specific virus (or group of viruses), and the other a non-specific chemical substance which enables the virus to infect. These two factors can be separated, and their properties studied. Irritation may, by some action, furnish the specific factor which allows the virus to infect. In conjunction with this paper J. E. Barnard publishes the photographs of these filtrable viruses taken by ultra-violet light. Because of the careful controls, the spherical bodies shown in the photographs are in all probability the viruses dealt with.

The virus of cancer, cultivated by Gye, and photographed by Barnard, is too small to be seen with the microscope in common use at the present time. Furthermore, the virus is smaller than the largest colloidal particles in the cell. New methods of research will have to be devised, therefore, before we can explore cytologically the possibilities opened up by the work of these investigators. The importance of Carrel's work has been described on page 229 of this issue.

Cytology of Cancer.—R. J. Ludford^{36/1x} discusses at length the etiology of cancer under the title, "The General and Experimental Cytology of Cancer," in which article he compares tumors with the culture of tissues. In both instances the growth is continuous, as long as the medium of the tissue culture is satisfactory, and sub-culture is adequately carried on. In this article are recounted many of the theories of the etiology of cancer. The embryonic rest theory of Cohnheim, which infers that certain cells fail to continue to divide at the same rate as their neighbors, during the rapid cell division that occurs in the early foetal life. These cells in adult life, for some unknown reason, suddenly take on their original speed of growth, and result in cancer. This theory answers fairly well for the teratomas and embryomas, but does not hold for the great majority of

new growths. The parasitic theory holds that a parasite causes this condition, and various parasites, from gross nematodes down to filterable viruses, have been apparently justly involved, though, in most cases, they have only been convicted of furnishing the irritation that seems to be the commonest factor of all.

Under cytological theories, this author describes the gametic theory, which supposes that the tumor cells have taken on the heterotypic mitotic form of cell division, common to germ cells. Under these conditions it is considered that the tumor cells, as in the case of the germ cells, have escaped the somatic control of the body, and multiply as a parasite, at the expense of the remaining tissues. This same urge in the gamete is directed to the formation of a new individual, which tends to exist in the fluids of the parent in the lower forms of life, and to carry a parasitic organ in the higher forms, which normally has almost malignant tendencies, in its ability to penetrate the tissues of the parent, in its voracious search for nourishment. This theory is original with Farmer, Moore, and Walker and suffers from the lack of proof of the existence of heterotypic mitoses in new growth. The other cytological theory, the chromosome theory of Boveri, suggests that malignancy results from an abnormal cell division which produces a cell whose chromatin content allows it to exist alone, while at the same time the factor which controls cell division has been lost. This shares the same criticisms as the other cytological theory.

The irritation theory of Virchow, which probably has the greatest number of followers to-day, considers that irritation, commonly of a low-grade, long-continued type, is responsible for a repeated urge on the process of repair phenomena, which finally results in an aberration of this function and the transition into the benign and malignant new growths. This theory answers the cytological requirements of benign and malignant tumors, and seems to illustrate cytologically in the repair of tissue the transition from the chronic inflammatory condition to tumors. It also embraces the parasitic theory, since some of the tumors of the lower animals are evidently secondary to microorganisms of some size, as the leptospira in the case of the experimental rat carcinoma of Fibiger, and the crown-gall tumors of plants described by Irwin Smith. This theory is in accord with the production of tumors by X-rays, tar, soot, oils, paraffins, and other chemical and

physical irritants. This theory also is supported by the incidence of cancer, which is greater in those organs which by their own functions are subjected to the type of irritation supposed to produce cancer, namely, the non-lactating breast, the lacerated cervix, the chronic stomach ulcer, and numerous other examples. This author also considers the theory of tissue tension, by showing in an excellent series of illustrations, how an excised piece of epithelium will regenerate itself, until the fault is filled, unless its urge to grow is greater than the tissue tension of the underlying connective tissue. In this same set of illustrations he depicts the principle of tissue culture, and shows its relation to the cytology of new growth, mentioning the function of the process of repair and its relation to cancer unless it is curbed by the parent organism. The writer omits some of the less attractive and somewhat discarded theories, and cites the theory as promulgated by Gye and Barnard above.

This author disclaims any definite cytological attribute characteristic of cancer, and goes into an elaborate analysis of the finer structure of the living cell, which is a splendid histological, physical, and mechanical description of this unit of tissue, and which includes all of our knowledge of this subject up to date. The author then cites the characteristics which determine the amount of malignancy a tumor has, stating that the nearer to the embryonic, and the farther removed from function the individual cells are in their internal make-up, as well as their arrangement to simulate organ complexes, the more malignant they are.

Of the various structures of the cell, he claims that the Golgi apparatus shows the greatest variation from normal in the cancer cell. This apparatus of the cell tends to keep the same form in the tumor that it shows in the normal cells from which the tumor originated, and illustrations are used to show that this variation is essentially quantitative rather than qualitative.

The variations as to polarity are shown in this article, and these are in keeping with the variation from normal function which the tumor shows. The amount of stroma a cancer or a tissue culture carries determines its polarity, the distribution of its mitochondria, and the approach it makes toward normal arrangement and function.

The hypertrophy of tumor cells is described as occurring in the stroma, as well as in the tumor cells, and is attributed to some growth-

promoting substance which acts more strongly on the cytoplasm than upon the nucleus, and which is probably the result of stimulation of the autolysins from necrotic tissue. The mechanics of the formation of Plimmer's bodies is well described and adequately illustrated. The wide variation of the chromatin content of tumor cells is discussed, and attributed to the marked increase of nuclear function necessitated by the rapid cell division. Nuclear fragmentation is taken up and is described as a distinct pathological process, probably of a degenerative nature. Brailsford Robertson is quoted as proposing that the asymmetrical mitoses are a factor in cancer, in that the daughter cell, with the more equal nucleo-cytoplasmic ratio, overwhelms those cells with the larger ratio, and cancer results. The occurrence of true amitosis in new growths is denied by this author, except possibly as a degenerative process. Giant cells are described as the result of the various defects of mitosis produced by the growth inhibiting substances of cancer, which are the factors which necessitate sub-culturing *in vitro*.

The formation of fat appears to be directly from the mitochondria, and that of pigment from the extrusion of chromogen masses from the nucleus. The author quotes Drew and others in the description of a growth-activating substance, which stimulates cultures to rapid growth, and which is found in greater quantities in the supernatant fluid of the more malignant tumors.

In conclusion Ludford says, "It has been pointed out that with our present microscopic technic there is no means of distinguishing between a normal and a cancerous cell. The wide range of pathological variations are the morphological expression of the reaction of the cells to the peculiar conditions of tumor growth. There is no pathological state restricted to cancer cells alone, so that there exists for the cancer cell no precise morphological diagnostic character of any kind."

Action of Oils in the Production of Tumors.—Burroughs and Johnson,^{11/ix} in an article on the action of oils in the production of tumors, claim that the factors of growth and function are balanced in a normal tissue, and that new growth represents a loss of this balance. The rapid growth of the embryo continues until the organism has reached the stage of function, then this growth urge is suppressed by the change in the quality and quantity of nutrition and this energy

is transposed into function. The normal amount of this growth urge left is only what is sufficient to take care of repair and regeneration. Then any thing which disturbs the function of a cell may alter its energies so that the small amount of growth necessary for regeneration and repair can be exaggerated to the speed of growth it possessed in the embryo, and cancer results. These authors have found that cell cultures give off an extract which stimulates growth, and that this substance acts quantitatively; a small amount stimulates cells to digest fats and proteins, while greater amounts cause the cell to divide, and still greater amounts cause the cell to digest itself. In cell cultures these authors have found that there is a direct relation between volume of tissue culture and the medium in which it is grown, and when this ratio is proper, the outer layer of cells migrates into the medium, the intermediate zones undergo mitosis, and the inner layers digest themselves, if the oxygen concentrations and the other requirements of tissue culture are maintained.

Burroughs and Johnson claim that this substance, which so easily diffuses through the media of cell cultures, is an oxidation product derived from the utilization of food. The single cell will not grow, because this extract from a solitary cell while it is growing is so diluted in the smallest amount of media that can be used, that the cell is not given the urge to undergo mitosis, when it has reached the volume-to-surface ratio proper for that particular cell to divide. This urge is provided when the right quantity of this growth-promoting extract is added and a single cell can thus be made to multiply. They found certain factors control the action of these elements of growth, and an ample supply of oxygen, and adequate means for this quantity to diffuse to all parts is essential. This quantity of oxygen was found to be about one-third the concentration of the air. The satisfactory diffusion thickness of tissue cells was found to be from 1 to 2 mm., and about half this distance for coagulated serum and plasma.

The conservation of the growth-promoting extract, sufficient to continue mitosis, is accomplished by crowding the cells together in the minimum of media, so that the measurements of tissue fragments will show no diameter greater than 2 mm., and of the plasma or serum media, none greater than 0.7 mm. A third factor is necessary for the growth of tissue cultures, both for normal tissues and for cancer transplants, this factor is stagnation of the media. The rota-

tion of migration, mitosis, and autolysis that occurs in cell cultures, as governed by the thickness of the different elements, because of its influence upon the diffusion of the oxygen, shifts to different areas, as the culture grows and alters these measurements. The factor of stagnation of the medium seems to conserve further the growth-promoting substance which these authors call "archusia," and avoids the necessity of furnishing this extract for new cultures from the fluids of old cultures. These authors call the urge which makes cells function, "ergusia," in contrast to "archusia," which makes cells divide. Ergusia is in the ascendancy when cells have their normal blood supply, stimulated to an active circulation by the proper trophic and sympathetic nerves as determined by the need within the organ or the demand on it by other organs. This adequate blood supply means sufficient nourishment as well as the adequate removal of wastes. Archusia replaces ergusia when cells are crowded together and stagnation of food and oxygen results, and the waste products are not removed. This reversion from function to growth, then, may be produced by those stagnation factors which are necessary for the multiplication of cells in cell cultures of normal tissues and of cancer transplants, and so new growths may result from such an alteration of their environment in organs.

These writers conclude that the lipid solvents produce cancer by attracting cells away from their blood supply and intercellular substances; this both crowds cells together and alters their oxygen and food supply, thus simulating the exact conditions to replace ergusia with archusia in tissue cultures, and cause them to forsake function for growth. Certain concentrations of archusia stimulate the release of ergusia from cells, which is a lipid-soluble substance, elaborated by cells to assist them to digest fats, and which acts as an attraction on oils when they are used as the irritation factor to produce cancer. These oils draw the cells to them, lower their surface tension, and by releasing their ergusia allow archusia to dominate, producing an unnatural mitosis. In this way they believe that any condition that can concentrate cells in the organism, so that the circulation is reduced enough to supply only the outer layers of cells with enough oxygen to divide and not function, leaving the centre of the mass to stagnate, and thus prevent escape by diffusion of the growth-promoting substance archusia, can produce cancer.

Pre-cancerous Changes in the Human Breast.—Sir George L. Cheatele ^{8/v} reports some valuable information, gathered by making complete serial sections of the whole female breast with a large microtome. By this method he has been able to follow single ducts from their acini to the nipple. One of the most important points that he brings out is that one duct and its acini alone may be the seat of papillomata, and the other changes due to local irritation that lead to cancer. Citing that the human breast is developed from the surface epithelium, he describes the skin changes that occur in tar workers and compares them with the parallel alterations in the epithelium of the breast due to irritation. In young tar workers the first change that occurs is a desquamative epithelial hyperplasia, with an accompanying round cell, and connective tissue increase beneath it. On continued exposure to the tar, papillomata result, whose epithelium is not desquamative in type, but which shows a true pathological proliferation which he designates as “dysgenetic.” These two changes occur in young individuals. The next type of lesion is a dysgenetic epithelial hyperplasia, which does not project above the skin, but is squamous in form, and represents a local thickening of it, without extending beyond the normal boundaries. The last event is the malignant change in this thickened squamous epithelium when it proceeds to rapid growth, breaks the normal boundaries and undergoes metastasis. This last change occurs in workers of forty-five years and over. The irritation due to X-rays produces the same changes, in the corresponding ages. Experimental tar cancer in the mouse follows the same sequence, occupying about a quarter of the lifetime of the mouse. To prove the potential malignancy of the third change described by the author, he cites the transplanting of this localized squamous hyperplasia in the mouse by Dr. A. J. Murray, with frank malignancy in the transplant.

All these changes occur in the breast, and in the same age cycles. In this organ there are two types of the first desquamative hyperplasia, one a diffused, generalized form which produces masses of degenerated, dried, flattened, and atrophied cells. The writer claims that this form is capable of causing considerable pain. The second type begins like the first in the terminal ducts and acini, is painless, and consists of an elongation of the epithelium, which results in a collection of colostrum-like cells, arising from these elongated cells.

This is accompanied by an increase of the peri-canalicular and the interacinous connective tissue, and occasional collections of lymphocytes occur. This process is one of the causes of cysts of the breasts and occurs in women of about thirty years of age. The next in the sequence is the formation of papillomata, which may affect a whole duct, as shown in the serial sections. The third form of this lesion is the dysgenetic hyperplasia, which looks malignant, yet does not break through the basement membrane, this the author regards as malignant, but which many writers designate as pre-cancerous or pre-malignant. The last series of events in this process is the frank cancer with its typical abnormal epithelial relations. The author derives his conclusions from the seeing of large numbers of complete serial sections of breasts, in which the phenomena of irritation can be followed through whole ducts. The writer objects to the use of the term "chronic mastitis," since he believes that there is little or none of the elements of inflammation in the process at any time, it being wholly one of hyperplasia. He also uses the term "pre-cancerous" for his third change of epithelial hyperplasia, but says there is no state of this condition which surely terminates in cancer.

This work is a very valuable one on this subject, and recalls to the pathologist countless lesions of the breast which illustrate these principles.

J. C. Mottram,^{17/11} in working with the cultivation of cancer *in vitro*, from normal rat kidneys exposed to radium and X-rays, and to tissue extracts of adult rats which have been treated with heat and X-ray exposure, concludes that the normal growth-inhibiting factor which exists in all normal tissues is destroyed by this method.

W. Cramer in the same issue concludes that the loss of enervation in an area of skin not only does not predispose to cancer, but the reaction of these peripheral nerves are an essential factor in giving chronic irritation the power to produce those changes in the blood supply necessary to the production of cancer.

Lead in the Treatment of Cancer.—W. B. Bell *et al.* have been working for several years on the curative action of lead on new growths, and have come to the conclusion that this metal has a high value in this disease. Colloid combinations of the metal are the best compounds to administer, and the intravenous route is safe if the compound is made by experts and administered in less than eight

hours. This prevents the sending of the substance any great distance to be used by others. The abstract below is part of the basic work which was started as the result of what seemed to be several definite cures, by this method. The selective action of lead upon the rapidly growing cells of the trophoblast is compared with the same action on the malignant cell, which has the same rapidly growing faculties coupled with the lack of defensive powers. This research has had a substantial endowment in Liverpool and is in the process of a complete evaluation by a large corps of competent workers.

Dr. J. G. Adami^{19/xi-21} speaks favorably of the work of Prof. Blair Bell upon the use of lead compounds in new growths, though he does not specifically indicate the method used, nor summarize the results. In this communication it is intimated that a large number of his colleagues know of the work, and that this knowledge was stimulating enough to cause a considerable endowment to be given and a large number of workers in different laboratories to offer their assistance in checking the work. This would indicate that the present year might see some information of value produced from these researches.

The following is an abstract of the first paper published in the series upon the therapeutic use of lead in cancer.

W. B. Bell, R. A. Hendry and H. E. Annett have attacked the problem of the genesis, nature and inhibition of malignant neoplasia by taking as a working hypothesis the idea that the invasion of the maternal tissues by the trophoblast of the fertilized ovum—a process which, if unrestrained, may develop into the most malignant manifestation known—resembles in its mechanism that of cancerous extension. In connection with this theory it has seemed important to demonstrate beyond all doubt that lead produces abortion by its action on the chorionic epithelium, that this action is specific, and that other metals and substances investigated have not the action. From animal experiments in which intravenous injections of lead, copper and thallium were employed it appears that lead has a selective affinity for chorionic epithelium, and that abortion can be produced by the action of lead on the fetal ectoderm (trophoblast) without the maternal organism being affected in any way. The effective aborting dose of lead is about half the lethal dose. The effects of copper and thallium are uncertain; there appears to be no definite quantity of lead which will inevitably produce abortion without damage to the mother; thallium is relatively atoxic. Abortion following the administration of copper or thallium is not due to specific action on the chorionic epithelium. It is the result of hemorrhage in the uterus, probably due to temporary vascularity incident to the pregnancy.

Diagnosis of Cancer.—Irwin Smith (*Science* for June 12, 1925), speaking before the American Association for Cancer Research, related considerable advance information from cancer centres in Europe

after a tour of that area of eight months. He cites a diagnostic method perfected by Kotzareff and Weyl, of Geneva, as yet unpublished, by which these investigators inject radio-colloidal substances into the blood stream of cancerous patients, with the result that the rapidly dividing cells of the tumor fix the radium to such an extent that they will affect a sensitive plate if exposed to it for a certain length of time (several hours), outlining upon the plate when it is developed the extent of the tumor. The only confusion this method gave was with young embryonic tissues, which defect is not of much moment, as it is fairly easy to rule out this one exception. Doctor Smith was also favorably impressed with the demonstrations of a serum diagnosis test for cancer shown to him by Doctor Botelho at the cancer clinic in the Hotel Dieu in Paris. This is a chemico-physical test which depends upon the action of nitric acid and iodine, on sera of the same specific gravity as determined by the spectroscope. Doctor Itchikawa verbally confirmed these results for experimental tar cancer in rabbits.

The results of irradiation in the various clinics visited do not seem to be different from those seen in the clinics of this country with an occasional exception of hyperenthusiasm, especially for the results in the easily reached tumors of epithelial origin. Doctor Botelho, of Paris, is using in inoperable cases a mixture of physiological salt solution, glycerin, tannic acid, iodine, and potassium iodide. This treatment controls pain and odor, sloughing off the cancerous tissue and not apparently injuring the normal layers.

Parasitic Theory of Cancer.—Smith is a strong exponent of the parasitic theory of cancer, having for years worked with the crown-gall tumors in plants. He states that the non-parasitic theory supposes that tumors are normal tissues with the growth-controlling functions lost, and that the parasitic theory holds that the cells are different and pathological because of the results of parasites or their products. Otto Warburg, of Berlin, has shown that cancer cells and other tissue cultures produce an excess of lactic acid in the presence of grape sugar, when grown anaërobically, but that the normal tissues can destroy this excess of acid when grown aërobically, while the cancer cells cannot. Warburg suggests that normal epithelium is a mixture of glycolyzing and oxidizing cells and that when there is a pathological condition which reduces the oxygen tension (pressure,

turgescence, anæmia, infection, etc.) the glycolyzing cells overgrow the oxidizing ones, and produce cancer. Irwin Smith believes with Burroughs and Johnson that reduced oxygen tension is a factor in producing tumor, stating that under this condition the "tumor must divide or be asphyxiated"; since "the cells breathe through their surface, and the smaller the cell, the greater the respiratory surface, in comparison with the amount of protoplasm to be aerated."

The writer states that Dr. Fridthof Bang, of Copenhagen, has observed a cancer of the nose following a single splash of hot tar, and has also produced two cases of epithelial cancer in mice, by a single burn with an electric cautery. This he holds as evidence against the irritation theory of Virchow.

Cancer Produced by Bacteria.—Dr. Ferdinand Blumenthal *et al.*, working in Berlin, have isolated from human breast cancers an organism which resembles culturally the *B. tumefaciens*, and with which he has been able to produce malignant transplantable tumors in rats, and crown-gall in plants. All of the material has been examined by Irwin Smith, and he states that this examination has dissipated the doubts entertained upon reading the article. These investigators have grown the organism on agar slants, it belongs serologically in the group with *B. tumefaciens*, is known as PM and continues to keep its identity and produces its lesion constantly. Pathologists vary as to the character of these tumors, some even claim that they are nothing but low-grade infections, of a chronic type, and that the nodules frequently contain typical macrophages, characteristic of this type of infection. Professor Fibiger, of Copenhagen, and Doctor Riechert, of Dresden, are working with these cultures, and appear to have been able to duplicate the work of Blumenthal.

It is evident from the literature that there is a strong movement toward the parasitic theory of cancer. In addition the chemistry and the physics of this condition are being rapidly advanced, and with them the physiology of the cell and the mechanics of cell growth are being cleared up. From the knowledge gained of these angles of tumors it seems that the greatest promise for cancer research lies in the realm of cytological investigation and tissue culture. That we are on the verge of the discovery of the etiology of cancer seems to be scouted by many conservative pathologists, and that we are about to discover its cure, by many more.

Irritation Theory of.—G. L. Rohdenburg^{29/III} sums up the basic facts which he believes have been demonstrated by the past research in cancer. These state that cancer begins in a susceptible tissue or individual after chronic irritation, the susceptible factors playing the most important part in the process. The chronic irritation may be supplied by any one of many irritation factors, such as parasitic, thermal, actinic, chemical or physical. Chemical investigations have failed to show any constant, fundamental differences between normal and cancerous tissue. The common occurrence of retrogression in experimental cancer and the occasional appearance of it in human cases have failed to show the usual immunological processes which should occur, if bacteria were the cause of new growth.

Parthenogenetic Theory of.—The basic difference between cancer and normal tissue is the unrestrained cell division of the former, and the author feels that all other apparent differences are merely the expressions of this one. Referring to the work of Loeb on artificial parthenogenesis in sea urchin's eggs, who produced the development of these animals from unfertilized eggs, by immersing them in an acid and then incubating them in hypertonic sea water, this writer claims that the acid solution causes the osmosis of electrolytes and water into the cell, which causes it to grow rapidly, and when the ratio of surface to volume is lowered sufficiently the cell divides. The hypertonic sea water furnishes the correct physical and chemical conditions for the further increase in growth and the consequent progressive increase in the speed of cell division.

Rohdenburg believes that the same physical and chemical alterations in tissues and tissue juices occur at the inception of every new growth. The irritation factor kills cells, producing the necessary acidity, and the autolysis which follows produces the excess of mineral salts and other nutritive substances in hypertonic solution necessary to keep up the vicious circle, which results in unrestrained cell division. Chronic irritation repeats this process, until the rapidly dividing group of cells contains an excess of mineral salts, large enough to overcome the ability of the circulation to furnish fluid nourishment enough to dilute the salt content and restore the balance. The mass then becomes chronically over-nourished, furnishing another urge to the vicious circle, and when the process assumes momentum enough, new growth results.

Numerous experiments are cited to show that there is a general demineralization of cancer patients, and the constant increase of the salt content of tissue in and around cancer transplants. These principles are cited for the susceptible and resistant strains of laboratory animals in cancer transplantation, those showing a high mineral and sodium blood content being easy to grow tumor on, while the opposite type are resistant to the process. It has been shown that resistance in susceptible animals can be raised by the parenteral introduction of living homologous protein before the introduction of the tumor transplant, and that this is accompanied by a demineralization of the blood stream up to 14 per cent. Dead homologous protein, and heterologous protein, both living and dead, hypermineralize the blood, increasing the sodium content by 11 per cent. Autologous protein produces a combination of these results, demineralizing the blood and raising the sodium content. The injection of living homologous protein does not influence the transplanted tumor once it has been firmly established in growth, nor does it alter the salt content, after there has been a proliferating mass of cells in the organism, even if that mass be represented by a simple pregnancy. Rohdenburg concludes that new growth is the result of a disturbance of salt metabolism, whereby the cell becomes mineralized to a greater extent than the surrounding body fluids.

Michael Levine ^{29/111} makes a very careful review of the literature on the cytology of cancer of plants and animals, and concludes that human cancer cells differ in size and mitotic division from normal cells. The many variations of cells in size and shape of nucleus appear in animal neoplasms, while this condition in the tumors of plants is an accident, and no variations in nucleus occur in these growths that do not occur in the normal tissue on the site of inoculation. All of the cells in plant tumors produced by infection pass through the phases of youth, maturity, and old age, and die independently of the host. This author presents a very convincing set of proofs indicating that there is little in common between plant and animal tumors.

A survey of the literature indicates that many of the sero-diagnostic measures advocated for cancer do not prove efficacious in the hands of others than the originators.

Sero-diagnosis in.—F. J. Laux ^{38/11-26} applied Kahn's cancer re-

action in 57 cases of various diseases without malignant tumor, with the result that there was a positive opalescent reaction in 22 cases. Among the diseases were sepsis, croup, pneumonia, tuberculosis, ulcer ventriculi, pernicious anæmia, periarteritis nodosa, pancreatic insufficiency, and intestinal polyposis. On the other hand, in a series of cases of malignant tumor the Kahn reaction was negative in 43.3 per cent., and positive in only 38.6 per cent. In the latter cases there was an advanced state of tissue degeneration and cachexia. From these and similar observations the author concludes that clinically the use of this reaction is surrounded with many reservations. It is often negative in the presence of malignant tumors and in cases in which no tumor exists it is often positive.

Jacques Lavedau^{50/11-21} reviews the literature of the sero-diagnosis of cancer. In 1910, Weinberg and Paltauf, reporting on the study of this subject, affirmed that "the hemo-diagnosis of cancer does not, as yet, exist." Ten years later Weinberg wrote, "In spite of a great number of published articles on the sero-diagnosis of cancer, it is impossible to point to a method which permits of the detection of the presence of specific antibodies in the serum of the host of a malignant tumor, as many as have been the studies by all modern biological methods." Likewise, recently Wolff concludes "that the examination of the blood is of no particular value for the diagnosis of cancer." Peyre points out "that all the serological reactions thus far proposed for the diagnosis of malignant neoplasms have scarcely any specific value; they give contradictory results which forbid their application." Sachs also says, "There do not exist any sero-diagnostic characteristics of tumors, for while cancer produces modifications of the blood serum, it produces no change presenting a specific characteristic." From a review of this nature one cannot reach any other conclusion than that set forth above. The multiplicity of sero-diagnostic methods suggested is proof in itself of the inadequacy of each of them.

Inhibiting Action of Fatty Acids and Their Salts in Experimental Cancer.—J. Lecloux^{24/x1-24} has studied the action of different fatty acids and their salts on the evolution of experimental tar cancer in mice. Two facts stand out clearly from these experiments. First, there is a delay in the appearance of the papillary cancerous process in mice which have received the oleate of soda; this delay averaged

from thirty to fifty days. Secondly, once a papilloma appeared, cancerization made its appearance rapidly, but the tumor did not reach a volume as great as in the controls. Lecloux believes it is the oleic radical and not the metallic ion which retards cancerization. The retarding action of oleic acid and sodium oleate seem to be the same. It also seems that the application of oleic acid does not modify in any way a papilloma already formed, nor does it arrest the progress of cancer. In this preliminary communication no attempt is made to interpret or explain the results obtained.

CARBON TETRACHLORIDE

Poisoning.—A comprehensive study of carbon tetrachloride poisoning carried out by George H. Gardner, R. C. Grove, R. K. Gustafson, E. D. Maire, M. J. Thompson, H. S. Wells and Paul D. Lamson ^{22/41} shows that this substance causes central necrosis of the liver when given by mouth, or by rectum, subcutaneously, intraperitoneally, and even when the vapor is inhaled. Lesions other than those in the liver are inconsequential after oral administration of CCl_4 . The smallest oral dose of this substance which will produce liver necrosis has not been determined. Definite lesions have been observed as early as twelve hours after oral administration of CCl_4 . The maximum lesion occurs about forty-eight hours after ingestion. Healing of the lesions begins three or four days after oral administration, and is not completed at the end of five weeks. The extent of the liver necrosis does not increase uniformly as the size of the dose. Puppies and rabbits are more susceptible to carbon tetrachloride poisoning than are adult dogs. Oral administration of alcohol with the CCl_4 increases the toxicity. Intraportal injections of CCl_4 produce only diffuse hemorrhagic liver necrosis. Injection into a peripheral vein produces foci of hemorrhage, œdema and an occasional area of necrosis in the lungs.

CHOLECYSTOGRAPHY

Oral Administration of Sodium Tetra-iodophenolphthalein.—In 1924, E. A. Graham and W. H. Cole (*Am. J. Med. Sci.*, lxxxii, p. 613) published a preliminary report showing how it was possible to obtain röntgenologic visualization of the gall-bladder. Since that time considerable progress has been made in the X-ray study of the gall-bladder that promises to be exceedingly valuable in the diagnosis of gall-bladder disease. In the preliminary tests made by Graham

and Cole, intravenous injections of the sodium salt of tetrachlorophenolphthalein were employed, but with this substance satisfactory shadows of the gall-bladder were not obtained. Because of the similarity of chemical structure, it was thought that tetra-iodophthalein would also be excreted into the bile and might cast a satisfactory shadow because of its iodine content. With this substance shadows of the gall-bladder were revealed, but the substance seemed to be too toxic to admit of its extensive use in man. After further experiments these authors advocated calcium tetrabromphthalein and more recently tetrabromphthalein. These observations indicated that the gall-bladder could be made opaque to the röntgen-ray by the intravenous injection of various derivatives of phenolphthalein. Experiments were then begun to determine whether it would not be possible to obtain shadows of the gall-bladder after oral administration of these compounds. Although the reactions to intravenous injection of sodium tetra-iodophenolphthalein, which these authors used for cholecystography, are few and of no moment, they have come to adopt the oral method of administration because of its simplicity and because it avoids the occasional severe reactions to intravenous injection of halogenated phenolphthaleins. Graham, Cole, Moore and Copher^{35/ix-26} relate their experiences with attempts at oral administration of various substances. It is known that the hydrochloric acid of the gastric juice precipitates the soluble sodium salts of the phthaleins in the insoluble acid form. It is also known that the sodium salts are absorbed from the intestine. Of this the authors have evidence because they obtained shadows of the gall-bladder after giving the salts by rectum. Shadows were also obtained after introduction of sodium tetrabromphthalein into the jejunum by laparotomy. Clinical application of these facts for cholecystography was made by the oral administration of sodium tetrabromphenolphthalein and later tetra-iodophenolphthalein in capsules coated with phenol salicylate. As phenol salicylate is not digested in the stomach it reaches the small intestine, where it is usually dissolved, freeing the contents of the capsule for absorption. Tetra-iodophenolphthalein is probably carried to the liver through the portal circulation, where it is excreted in the bile, producing the shadow of the gall-bladder just as after intravenous injection. The dose of sodium tetra-iodophenolphthalein by mouth has, in the work of these authors, averaged 0.07 gm. per kilo of body-weight in man. They

have given 5 gm. as the routine dose for an adult. It has been given in capsules or pills coated with phenol salicylate, containing 1 gm. of sodium tetra-iodophenolphthalein. The dose may be further subdivided if desired. The five capsules or pills are taken a few minutes apart in the course of the evening meal near 6.30 P.M. Food is withheld until after films are made at 9 A.M. and 1 P.M. the following day. After these röntgenograms have been made, a glass of milk or a cup of coffee may be given. Another film of the gall-bladder region is made at 5 P.M. and sometimes again at 9 A.M. the next morning. The evening meal is eaten as usual. The technic is the same as for other cholecystograms. Among 112 cholecystography patients, 4 per cent. were nauseated and vomited; a few others had mild discomfort. There were no toxic symptoms attributable to phenol salicylate. The authors have performed cholecystography on a total of 467 hospital and ambulatory patients. A correct diagnosis has been made in 95 per cent. of the cases confirmed by operation. These authors estimate that at the time of writing several thousand cystograms have been safely made. In some cases there have been slight reactions of nausea or vomiting. Caution should be observed in injecting patients with cardiac lesions.

Lester R. Whitaker and Gibbs Milliken have devoted considerable attention to study of cholecystography, publishing their results in *Surgery, Gynecology and Obstetrics* (1925, Vol. 40, pages 17, 646 and 847). By animal experiments they have tested the toxicity of sodium tetra-iodophenolphthalein and sodium tetrabromphenolphthalein, and found no appreciable toxicity of the two drugs. In practice nearly twice as much of the bromine salt as of the iodine salt is required to obtain a shadow of the gall-bladder; consequently there is a wider margin of safety in favor of sodium tetra-iodophenolphthalein. Whittaker and Milliken follow a method of administering the sodium tetra-iodophenolphthalein slightly different from that of Graham and Cole. They start at 8 P.M. and give four pills (5-grain salol-coated pills) every fifteen minutes until twenty pills are taken. A large dose is given in order to insure shadows. The patient lies on his right side during the period of taking the pills, and for an hour or more thereafter. Röntgenograms are made from twelve to fifteen hours after taking the pills. After the fifteen-hour film the patient eats a meal, and a hour afterward more röntgenograms are made.

The purpose of taking films after the meal is to see if the gall-bladder shrinks down during digestion, which indicates that the gall-bladder wall maintains its contractility.

Quite extensive observations on this subject have also been made by William H. Stewart, Max Einhorn and Eric J. Ryan.^{49/vii} They are convinced that the oral method of administering sodium tetra-iodophenolphthalein is the safest and best. They prophesy that in time it will prove to be as reliable in the röntgen investigation of the gall-bladder as bismuth and barium are in the intestinal tract. Even now it is possible to discover not only whether pathology is present, but to give, in addition, some definite data as to the size, shape, location and emptying power of the gall-bladder, and of no small importance is the ability to study the function of the liver, recognizing delay. These authors have experimented with the intrajejunal method of administration of the drug (introducing it into the jejunum through the duodenal tube). Samuel Weiss^{5/iii} and Israel O. Palefski have appeared to advocate this method. The latter writer^{47/xi-18} states that if a shadow is not obtained by the oral method or when the veins are not distinctly visible, the intraduodenal method may be used with advantage. He also points out that, contrary to expectations, sodium tetra-iodophenolphthalein does not always visualize non-opaque stones, neither are early cases of cholecystitis recognized by this test. Many normal gall-bladders are not visualized after oral administration. The results in such cases must be checked up by the other methods. The intravenous method is not followed by general or local effects and gives most dependable results. The literature contains reports by many writers who have investigated these new methods of cholecystography, which most certainly are rapidly taking a place among recognized diagnostic procedures.

COCAINE See **PSICaine**

DENGUE FEVER

Transmission of Dengue Fever by Mosquitoes.—Upon the willing shoulders of Colonel J. F. Siler rested the burden of getting out the laboratory findings of the Chief Surgeon's Office in the A.E.F., and he carried out his official duties with a smile which made all those with whom he came in contact do their utmost to lighten his difficult and onerous work. We can well imagine, therefore, how cheerfully Majors M. W. Hall and A. P. Hitchens,^{35/iv-18 :51/i & ii-1926} also

members of the U. S. Army medical department research board, and the volunteer soldiers to be infected with dengue, helped him in carrying on an important investigation of the dengue question in Manila in a ward of the Sternberg General Hospital between July, 1924, and July, 1925. Sixty-four volunteers of the Army force lent their bodies for inoculation experiments and in fifty-two instances (81 per cent.) dengue was produced by permitting infected mosquitoes to bite them. The strain from which the virus for experimentation was derived was passed from man to mosquito and back to man through six generations. Neither attenuation nor increase in virulence was experienced. In experiments made with eight volunteers it was found that the incubation period extended from the eleventh to the fourteenth day after infection. In experiments on twenty-one volunteers it was shown that the dengue patient is infective to mosquitoes during the late prodromal stages of dengue, six to eighteen hours prior to onset, and thereafter for the first three days of his disease. For the protection of others, great care should be taken that the *Aedes aegypti*, which is our old yellow-fever enemy, the *Stegomyia fasciata*, under a new name, does not have access to those affected during these periods. The infected mosquito, which bites during the day time, is able to transmit the virus eleven days after its infection and remains infected throughout its entire life of about six weeks' duration. Hereditary transmission of the virus did not occur in these experiments nor were the trials with *Culex quinque-fasciatus* as a transmitter of dengue successful. Freshly bred *Aedes aegypti* did not bite willingly at the time of their emergence, but after they had taken food and had been fertilized they took blood freely. This mosquito breeds with preference in human habitations, and deposits its eggs, which normally take three days to hatch out, in clear water. Uncovered receptacles should not be permitted within the houses and all adult mosquitoes noticed about the house should be destroyed. Aside from spoiling the habitat of the *Aedes aegypti* with the cooperation of the inhabitants, who should be instructed on the life history of the mosquito, maps should be made of the portions of the city or country where dengue shows endemic character. Dengue has no mortality in the Philippine Islands and infrequently attacks the native population to a noticeable degree, while recently arrived Caucasians suffer from it considerably. Three of the worst epi-

demics ever experienced by American troops were those in 1920, 1923 and 1924. In twenty-one years the number of days lost from duty by military personnel because of dengue approximated 7000 days a year. The dengue season, which in Manila usually extends from April to November, ending when the temperature falls below 50° F., is dependent upon the number and the time of the appearance of the *Aedes aegypti*.

DIPHTHERIA

L. Martin, G. Loiseau and Albert Lafaille^{21/vi-12} report that they have immunized 275 children between the ages of eight and eighteen years. Two injections of 0.5 and 1 c.c. of diphtheria antitoxin were given at an interval of fifteen to twenty-two days. In order to simplify the procedure, the Schick test was made twenty-one to twenty-nine days after the second anatoxin injection. The reaction was negative in 222 of 231 children tested; it was positive in six and slight in three. This procedure was carried out in several groups of children in a contaminated environment during an epidemic of diphtheria and under these conditions the test provoked active but temporary reactions. In the presence of an epidemic of diphtheria it is better to use the purified antitoxin first and then to vaccinate with anatoxin. The experience of these authors with anatoxin vaccination confirms that of other investigators. They find that children bear this form of vaccination well, especially those who are susceptible. With such patients it is needless to employ the Schick test, since three immunizing injections almost certainly protect in every case. Adults react markedly to the anatoxin injections, and in them the Schick test should be applied first, and only the positive reactors should be vaccinated.

Actions of Cardiac Stimulants in Circulatory Failure Due to Diphtheria.—Edmundson, Cooper, and Robert,^{35/xii-5} working with laboratory animals, found that the cardiac stimulants should be started early in prospective failures of circulation from diphtheria. Digitalis and pituitrin were found to be the most valuable drugs up to the time of collapse when warm intravenous glucose in 10 per cent. solution was found to have a dramatic life-saving effect. The cardiac stimulants continue their physiologic effect after the collapse has answered to the intravenous glucose.

DWARFS See MONGOLOID DWARFS

DYES POSSESSING THERAPEUTIC VALUE

I. C. Brill and H. H. Myers^{35/III-21} carefully recorded the blood-cultures and symptoms in five clinical cases of sepsis treated with intravenous mercurochrome and gentian violet, and from these findings conclude that these dyes had no influence in checking the progress of the infections. Using the maximum safe concentrations of these dyes in the blood stream, these workers tested their action *in vitro* upon staphylococcus, streptococcus and colon bacillus and conclude that three hours' exposure produced no bactericidal action on these organisms.

On the other hand, J. R. Ariza and B. M. Phelps (Thirteenth Annual Report of the Medical Department of the United Fruit Company) report the use of mercurochrome intravenously in practically every septic or infectious condition found in the tropics for which there is no specific treatment, claiming rapid and substantial benefit in the majority of their cases. These investigators employed a 1 per cent. solution and used 10 to 15 c.c. on from one to five days. Pneumonia and complicated gonorrhœa seemed to answer best to this treatment. C. M. Winn (*ibid.*) reports twenty-six cases of pneumonia in which this treatment was employed, with a death-rate of less than 20 per cent., whereas this death-rate for that locality for the preceding five years averaged 49.13 per cent.

ECTOPIC PREGNANCY See PREGNANCY

ELECTRICITY

Betton Massey, before the midwinter meeting of the Electrotherapeutic Society, pointed out the value of wave currents in intestinal activity. He says the choice of wave to stimulate muscles and glandular neurons cannot be made by choosing the wave by name, whether induction, surge or galvanic sinusoidal, but by the selection of a wave which, when it reaches the intestinal muscles or the neurons through the overlying resistance of skin, fat, and so forth, shall be strong enough to cause excitation, in spite of the scattering diffusion. The following conditions are important: If the height of voltage is immense, as in the static wave, the overlying resistances are negligible and the amperage may be slight. If the voltage and amperage are moderate, the slant abrupt but round, overlying resistances must be lessened by large, thoroughly moist pads, and the current increased to a point where sufficient amperage reaches the desired structures, this

being possible because of the sine curve lessening pain. Under these circumstances, waves of modern generators, such as the Morse, will stimulate intestinal muscles and neurons of abdominal glands when applied through the abdominal wall. In all cases it is not the wave delivered by the generator to the electrode plates that should be regarded as our therapeutic agent in percutaneous application, but the proportion of the wave that, overcoming the resistance of the skin and omentum, and in spite of wide subdermic diffusion, actually reaches the organ we wish to stimulate. It is important that one employ large currents, through large electrode pads that are thoroughly moist and make good contacts, to get effective action when using low-volt waves.

Becoming convinced from his personal experiences and from those of others that there is more to be obtained in the treatment of malignant disease than the direct killing of the cells of the neoplasm, Douglas Morgan has made radical changes in his technic. Continuing with the same kilovoltage (220) as before, and with the same milliamperage (4), distance (50 cm.) and filters (0.75 mm. Cu, and 1 mm. Al), the time factor was reduced very materially, namely, three to five minutes twice daily for tumors lying within 5 cm. of the surface, and five to ten minutes once or twice daily for those lying more deeply. The object in the choice of such a small dosage was to depress the most delicate embryonic neoplastic cells without injuring or depressing the normal surrounding cells; rather to stimulate these latter, causing leukocytosis, which is now considered to be such an important factor in the cure of cancer. Distinctly small doses act as a stimulus to the lymphogenic organs, causing lymphocytosis. If there is any basis in the suggested production of intercellular ferments (Ewing), or of the presence of antibodies in the blood, small doses are essential if the beneficial reactions of these are preserved. Another innovation in this author's technic is the adoption of large portals of entry, no attempt being made to prevent overlapping of areas. He still uses the cross-fire technic in order to irradiate the neoplasm from all sides and to stimulate as much of the normal tissue as possible. That these small doses have a definite potency has been amply demonstrated by the splendid results in cases that have received no previous irradiation, whether in superficial lesions, such as carcinoma of the breast, or in deeply lying lesions in the pelvis or the abdomen. The

beneficial results have been particularly striking in several cases which have previously received heavy irradiation without apparent benefit.

GNORRHŒA

After a study of 243 cases of gonorrhœa in women with reference to the relation of clinical findings to the question of the patient's infectivity or recovery, W. G. Schultz ^{64/xi-7} concludes as follows: Simultaneous infection of the urethra and cervix occurs in nine-tenths of the cases; a rectal gonorrhœa complicates the genital infection in three-fourths of the cases. There is apparently no difference in the localization of gonococci in parous and non-parous women. Only in those who were very old, very young, or else pregnant, was the vaginal mucosa affected. Before taking smears from the cervix and urethra for examination, the urethral opening and the external os must be carefully cleansed. A urethral specimen must not be taken until at least two hours after urination. In obtaining smears, the platinum loop, in Schultz's opinion, is insufficient; he finds a blunt spoon the best instrument for this purpose. In reaching a conclusion as to freedom from gonococci, fewer than five negative smears are inadequate. Even then stimulation of the suspected site of the lesion should be practised, preferably by a combination of physical, chemical and biological measures.

HEART

Ischæmia Cordis Intermittens.—Under the above terminology, L. Bischoff ^{39/x-10} describes a group of anginoid phenomena, which affect patients between the ages of thirty and seventy years. It is encountered mostly in males, after exercise. The affection is characterized by a disagreeable pain behind the sternum, which passes into a feeling of spasmodic contraction and oppressive sensations of anxiety, culminating in such a feeling of annihilation that the patients are obliged to stop their activities. In some instances it leads to complete unconsciousness. Often after a rest of a few minutes the patient is able to continue his walk in perfect comfort, but soon after the resumption of exercise the pain returns. The same phenomena are revealed in the history of all patients. The affection is distinguished from angina pectoris by the fact that it occurs during exercise, while angina pectoris occurs at night or during rest. The complex of symptoms under discussion is connected with an insufficient blood supply to the heart-muscle. In these cases, as in the

usual angina, the prognosis will depend on the etiology of the ischæmia, that is when there are alterations in the vessels, on the extent of such alterations, on the state of the aorta, of the heart-muscle, and its reserve power. Bischoff says he has never heard a double first sound in ischæmia cordis intermittens, while it has been repeatedly observed in angina pectoris. In one case fluoroscopic observations were made during an attack of ischæmia cordis intermittens and no alteration worth mentioning was noticed; the apparent pulsation and the well-visible range of contractions were small.

The Use of Urea as a Diuretic in Advanced Heart Failure.—J. Hamilton Crawford and J. F. McIntosh^{12/x} report their experience with the administration of urea in advanced heart failure. They gave urea in doses of 30 to 60 gm. a day to a small group of patients and then estimated the urea in the blood and urine and the chloride in the plasma. The result was a marked increase in the urine volume. The drug was particularly useful in cases in which adequate excretion was not maintained after the œdema had been decreased by other measures. In some cases it reduced the œdema when other remedies had failed. The increase in the urine output followed closely the curve of urea excretion. With continuous administration of the drug the daily volume of urine was maintained at an almost constant level. The response to the drug was rapid, but unless the dose was repeated its effect passed off in a short time. The changes in the urea excretion and the urine volume were found to be dependent upon the concentration of urea in the blood. In several cases in which there was a subnormal index of urea excretion which seemed to be due to the advanced heart failure, the index tended to improve with this treatment, and at the same time there was a general improvement in the clinical condition. No toxic symptoms were noted. These observations indicate that urea is a useful diuretic in cases of heart failure with œdema, in which treatment of the heart condition has failed to maintain adequate excretion.

The Selection of Patients with Angina Pectoris for Sympathectomy.—During the past year a number of observers have reported their results showing that sympathectomy affords striking relief to some patients suffering with angina pectoris. Samuel A. Levine and Francis C. Newton (*Amer. Heart Jr.*, Oct., 1925) stress the point that proper selection of cases ought to diminish markedly the immediate

surgical mortality. This selection should be so directed that those who are operated upon continue to live for an appreciable length of time to enjoy their improved health. Before operation is undertaken it is absolutely necessary that accurate diagnosis be made and that cardiac infarction be not confounded with angina pectoris. Furthermore, each patient should be studied to determine that there has not been any congestive heart failure, that the musculature of the heart is satisfactory and preferably that there is no valvular disease. In the author's seven cases selected for sympathectomy, all were alive three months to two years after operation. Three were rendered absolutely free from anginal attacks and have remained so; three continued to have typical anginal attacks but were nevertheless considerably improved, in that it required a greater effort to bring on the attacks. One patient was neither better nor worse. These writers urge that cases be reported in detail so that it will be possible to form a judgment as to the type of patients to be selected for operation.

HEREDITY

Halsey J. Bagg^{1/x1} continues his important work on "Hereditary Abnormalities of the Viscera," now covering a series that has occurred in the descendants of a group of 1800 autopsied X-rayed mice. His conclusions are: (1) Inherited abnormalities of the viscera have been noted in the descendants of a group of mice treated with comparatively light doses of unfiltered X-rays on five consecutive days. (2) The visceral abnormalities are mainly defects of the kidney, which may vary from a partial, to nearly complete atrophy of one kidney, to the congenital solitary-kidney condition, and to complete absence of both kidneys. The right or left kidney may be affected with equal frequency, and there is apparently no sex difference in this respect. (3) Animals with the congenital absence of both kidneys are born alive and are apparently of average weight and development in other respects. They live for about twenty-four hours. (4) Congenital hydronephrosis and polycystic kidneys are apparently associated with embryological factors that produce the suppression of kidney development. (5) Blindness and various defects of the limbs, syndactylism, polydactylism, and especially club-feet, are closely associated with abnormalities of the kidneys. One instance of *situs inversus viscerum* has been noted. (6) In the animals herein reported there is apparently a general tendency

to disturbances in embryonic development. (7) Embryological studies of young from strains with a high incidence of visceral abnormalities have shown that these defects are associated with blood extravasations, especially in the liver and testes, which are similar to those extravasations closely associated with the production of blindness and club-feet. (8) Selection has greatly increased the number of animals with visceral abnormalities in the experimental lines. (9) The visceral defects are definitely inherited, recessive to the normal, and when considered as one of the manifestations of a general tendency to abnormal structure, they approach the mendelian expectation in behavior.

INSULIN

Anaphylaxis from Its Administration.—M. Raynaud and A. Lacroix ^{21/v-29} report the case of a diabetic woman, aged sixty-one, who, after the injection of insulin, developed on several occasions signs of severe anaphylaxis. These consisted of marked œdema of the face and pharynx, generalized pruritus, abundant frothy mucus, headache and dyspnœa. The symptoms lasted about two hours. The authors endeavored to ascertain in how far the reaction was due to insulin and how far to other protein substances. They conclude that the insulin was responsible, causing hemoclasia. This, they point out, would explain certain alterations which were noted in the coagulation time of the blood and in the blood-pressure.

Intratracheal Injection of.—After performing experiments on the effectiveness of insulin when given by intratracheal injection, Heubner and Jongh ^{38/xii-24} made observations on the effects of inhalation of insulin. They used Netherlands insulin (organon)—not the solution with tricresol sold commercially, but a dry insulin, which was dissolved with just barely the amount of acid necessary to make a solution (pH 3 to 4); 5 per cent. glycerin added to this made it absolutely non-irritating. As an inhalation apparatus they used two new modifications of the Hirth inhalator (driven with oxygen from tanks), or the Draeger-Spiesschen drug atomizer (driven with the atmosphere compressor). As evidence of an insulin action a fall in blood-sugar, at least 0.1 mg. to the cubic centimetre, was seen in normal individuals. Both in normal individuals and in diabetics an insulin action can be brought about by inhalation, and to a certain extent the effect can be controlled. About thirty times as much

insulin is necessary as on subcutaneous injection. A more accurate dosage should be easily attainable, but it will require further experiments to show whether a more economical method can be devised.

Milk Secretion in Ewes from Its Use.—I. I. Nitzescu and G. Nicolau ^{24/xii-27-24} administered insulin to two ewes, three times a day subcutaneously. The first ewe, on a dry diet, presented almost the same variations in milk secretion on the days when insulin was administered as on days without insulin. In the second ewe, on a fresh diet, there was a slight diminution in the milk secreted after the injection of insulin, especially after the evening dose of insulin. This decrease in milk secretion seemed to be maintained on the following day. The percentage of fat, which frequently varied normally, showed, after the administration of insulin, a slight increase, sometimes quite marked. This was particularly noticeable on one occasion when the animal had an insulin convulsion. The percentage of lactose showed a remarkable invariability during the days without insulin. After insulin the quantity of lactose diminished, particularly after the evening dose, and this diminution persisted, though less markedly, on the following day. The lactose continued to be reduced in amount even though the hyperglycæmia fell to normal. The nitrogen of the casein and the total nitrogen of the milk were but slightly and irregularly influenced. The inorganic phosphates were slightly increased, especially in the second ewe, and the increase was maintained to a certain extent on the following day. These results agree in the main with those obtained by Giusti and Rietti in experiments on two goats.

Insulin in Pernicious Vomiting of Pregnancy.—Le Fevre ^{31/iii} reports good results in the pernicious vomiting of pregnancy with the use of insulin, combined with glucose. He uses the glucose in higher concentrations than others, combining it with one to two units of insulin per gram, in a 50 per cent. solution. By this method the solution can be administered with the usual, large, ground-glass syringe. Ten grams of glucose with its accompanying ten to twenty units of insulin can thus be handled in a 30-c.c. syringe, and used daily until the symptoms are controlled.

IRRIGATION

Charles W. Cathcart ^{19/xi-21} refers to the difficulty that has been encountered in obtaining a satisfactory method of intermittent irri-

gation with an automatically discharging siphon or by slow dropping of the fluid and he describes a device by which it is possible to secure accuracy as to the amount and regularity of the irrigations. It possesses the additional advantage of saving a great deal of work on the part of the nurse. The apparatus consists of clockwork run by electrical mechanism. The mechanism holds a valve open for a definite period of time at intervals desired by the surgeon. The valve can be adapted to deliver $\frac{1}{2}$ oz., 1 oz., or 2 oz., according to the aperture of exit given to it. There are various apertures which can be adjusted to the valve by means of separate nozzles. The clock by its control of an electric circuit can open the valve as often as is desired. This device has been tested on a severe case of compound fracture of the tibia, infected with *Bacillus pyocyaneus* at the Royal Infirmary, Edinburgh, and found to irrigate the wound satisfactorily. At the end of a fortnight the patient had improved to such an extent that the apparatus was no longer required. This is a valuable mechanical adjunct to the Carrel-Dakin treatment.

KALA-AZAR

S. R. Christophers, H. E. Shortt and P. J. Barraud of the Kala-azar Committee^{26/7} report the result of the dissection of 17 sand-flies fed on kala-azar cases. The flagellates which they found had the characters of cultural forms of *Herpetomonas donovani*, and in stained preparations closely resembled forms seen in cultures on about the third day. Forms apparently showing early stages in the formation of the flagellum, etc., were seen in one of the flies dissected on the third day, while in the flies showing numerous flagellates these all gave the appearance of active multiplication. The authors feel that there can be no doubt that these flagellates are developmental forms of the parasite of kala-azar. The formation of flagellate forms and multiplication such as occurs in culture may be considered as occurring in the sand-fly, *P. argentipes*, with some regularity when these insects are fed on the blood of kala-azar patients. The authors note, however, that the search for these flies in houses harboring cases of kala-azar has been almost negative.

KIDNEY See PREGNANCY

The Results of Experimental Work on Renal Function with Morphine and Atropine.—In carefully controlled experiments on human cases in kidney elimination tests with the usual dyes, Haines and

Milliken show quite conclusively that morphine and atropine help rather than hinder kidney function. Using laboratory animals, they ascertained that ether anæsthesia inhibited kidney function to a considerable extent, and that this inhibition was prevented from taking place by the preliminary injection of morphine and atropine. They report the same action in humans and suggest further experiments to increase the information along these lines. The combined drugs simulate denervation of the kidney in experimental animals. Thirty minutes of ether, in both humans and dogs, produce complete inhibition until the ether is stopped. Morphine and atropine before the ether completely prevent this inhibition. This information is invaluable, and gives logical reasons for an important procedure formally resting on a purely empirical basis.

LEAD See TETRA-ETHYL LEAD

LEAD TREATMENT OF CANCER See CANCER

LIVER

Functional Tests.—During the past year considerable attention has been centred on a study of the clinical value of the various tests used to determine the degree of impairment of liver function. The comparative value of some of these tests has been studied by Howard F. Shattuck, John C. Browne and Marjorie Preston.^{4/x} The tests studied were the Rowntree-Rosenthal, the estimation of bilirubinæmia by the icterus index of the blood, the van den Bergh bilirubinæmia test and Fouchet's test. In the author's hands the latter test proved unreliable for detecting minor grades of bilirubinæmia. In other respects the van den Bergh test served very well in its place, and has distinct value in studying liver function and jaundice. Positive results with both reactions indicate impaired liver function, but the extent must be determined by the icterus index or dye test. The van den Bergh test helps as a specific qualitative test for bile-pigment to control readings of the icterus index in the zone of latent jaundice; it distinguishes between hemolytic and obstructive jaundice. This study indicated that the icterus index is the most useful single functional liver test that is available for clinical work. Its greatest value is in the diagnosis of cholecystitis and cholelithiasis without clinical jaundice. It is a distinct aid in distinguishing between obstructive jaundice due to malignancy and catarrhal jaundice by show-

ing whether the jaundice is increasing, stationary or diminishing. It is helpful in the diagnosis of cirrhosis and malignant metastases in the liver, though apparently less so than the dye retention test; it may indicate the degree of cardiac decompensation, and the toleration of the liver to carbon tetrachloride, and to arsenicals in the treatment of syphilis. It will determine whether obstructive jaundice has been relieved by operation. It will help to differentiate the primary from the secondary anæmias. While these writers find the Rowntree dye test of supplementary value in measuring liver function, for clinical work they consider it more complicated, more objectionable to the patient, and not entirely free from danger. It seems to be of greater value than the icterus index in the diagnosis of cirrhosis and malignant metastases in the liver; in surgical cases with jaundice, the dye test helps to determine the damage to the liver parenchyma, and hence the surgical risk. Its greatest value is in the diagnosis of liver disease in patients without jaundice.

In a clinical and operative study of the icterus index by John V. Barrow, Eugene L. Armstrong and William H. Olds,^{4/x} they, too, find that the icterus index is the test of choice for the quantitative estimation of bilirubinæmia, and that there is no untoward effect or danger to the patient from its use. The Widal hemoclastic crisis probably tests the proteopexic function of the liver, which is allied to, but different from, the bile-forming function. They think it probable that the leukocyte tests of to-day may be in reality liver function tests. Extreme leukocytosis in the presence of bile is probably the result of a high-grade hematopoietic stimulant acting not because of the presence of bile, but in spite of it. The icterus index is a valuable aid in diagnosis, prognosis and treatment, but it is neither infallible nor specific in the diagnosis of any one disease, but as other clinical tests are rated this one has a high marking.

Quite recently Sanford M. Rosenthal and Edwin C. White^{35/iv-11} have published a new dye test for hepatic function, which they claim is safe, non-irritating and an accurate guide to the degree of impairment of liver function. After experimenting with various dyes, these authors found that bromsulphalein (phenoltetrabromphthalein sodium sulphonate) seemed to be ideal for testing liver function. Normally it is rapidly removed from the blood stream through the activity of the liver-cells, since in animals where the liver is extirpated, it is retained

in the blood stream almost *in toto* during the early period following its injection. It thus possesses striking advantages over phenoltetrachlorphthalein which, when injected in rabbits, is excreted to the extent of only 5 to 10 per cent. in one hour, and which never reaches high concentration in the blood.

In the Rosenthal test with bromsulphalein the patient is weighed and the dosage calculated on a basis of 2 mg. per kilogram of body-weight. The body-weight in pounds divided by 55 will give the exact quantity in cubic centimetres of the 5 per cent. solution required. It is injected directly into an arm vein. Thirty minutes after injection a sample of blood (4 or 5 c.c.) is drawn preferably from the opposite arm, by allowing the blood to run through a needle directly into a dry test-tube. After the blood has coagulated it is centrifuged and the clear serum is pipetted into two small test-tubes. To one of these is added one or two drops of 10 per cent. solution of sodium hydroxide to bring out the color of the dye, and to the other tube a drop of 5 per cent. hydrochloric acid to clear the serum of any hemolysis. The amount of dye present is estimated by direct comparison with a series of standards. In 20 cases of liver disease studied by this test, retention of dye in the blood thirty minutes after its injection varied from 3 to 99 per cent. Since it is normally absent from the blood at this time the percentage of retention that occurs may be interpreted directly in terms of percentage of impaired function so that 10 per cent. retention means 10 per cent. impairment.

LIVER EXTRACT See BLOOD-PRESSURE

MONGOLOID DWARFS

C. B. Davenport and Grace Allen ^{33/v1} find the following elements favorable to the production of mongoloid dwarfs: First, mothers who are constitutionally hypothyroid; second, advanced age when the thyroid and some other incretory glands are relatively inactive; third, overdrafts on the incretory system by excessive child-bearing; fourth, disturbance of endocrine balance by severe emotional disturbance; fifth, physical disturbances which may influence the quantity and quality of the fluids received by the foetus. Not all of these elements are present in the production of any mongoloid dwarf; but apparently two or more of them ordinarily are; and the combination of three or more of them increases the liability to the birth of a mongoloid dwarf. Such dwarf then appears as a child who did not

receive essential developmental impulses during foetal life and is not provided with an endocrine mechanism for making good entirely these deficiencies in later life.

MUMPS

A Spirochæte the Possible Cause of Mumps.—Yves Kermorgant, 7/vii of the Pasteur Institute of Paris, has published an article in which he describes a spirochæte which he finds in the saliva of mumps patients. This organism is of strikingly regular spiral form. It is ciliated and actively motile in young cultures, rotating about what may be called the fixed axis of its coils, and also making the irregular movements common to most spirochætes. It is grown anaërobically without difficulty in a medium containing rabbit serum and horse corpuscles. By passing the organisms through mediums containing horse serum most of the contaminating organisms are eliminated, with the exception of a motile, Gram negative bacillus that seems to have a true symbiotic relation with the spirochæte, possibly by influencing the reaction of the medium. This organism resembles somewhat *Spirochæta pallida* and *Spirochæta cuniculi*, though these organisms are not spiral, are soluble in saponin, and evidently differ serologically. The spirochæte found in mumps multiplies by transverse division, sometimes regularly in typical spirochætes, and sometimes irregularly into short forms and granular forms that are filterable, that can produce typical spirochætes in cultures with the living symbiotic bacilli, and that probably constitute a phase in the developmental cycles of the organism. This cycle corresponds well with certain characteristics of sub-cultures, which grow best only at a period of twenty-five to thirty days after the inoculation of the original culture. When cultures of these organisms are injected into the testicle or parotid gland they produce orchitis and parotitis similar both to the disease as it occurs in man and to the changes produced in animals by the use of saliva directly from mumps patients. Both rabbits and monkeys react to injections of these spirochætes, and while none of these organisms was found in sections of the glands, cultures of them contained many spirochætes. By the use of affected glands the infection could be passed along, but there was evidence of weakened virulence. The incubation period after injection of cultures is only from two to four days. It has been found that serum from convalescent patients after the third week agglutinates this spirochæte in higher dilutions

than it does other spirochætes, and the agglutination titre is increased notably by the sixth month. The serum of syphilitic patients and other anti-spirochæte serums agglutinate the organism only slightly and have no effect on its symbiotic bacillus. The serums of convalescent patients also show specific lysins. Living cultures attenuated by the addition of horse serum seem to produce immunity to subsequent inoculations with active virus. It is too early to state whether a protective and curative serum against mumps and an active vaccine can be obtained.

NOVASUROL

Novasurol, a New Diuretic.—An organic compound of mercury (sodium-oxymurcuric-ortho-chlorphenol oxylacetate with dimethyl malonylurea) has become well known in the treatment of syphilis, but its use in the treatment of some forms of cardiac failure comes as a new suggestion. A. R. Gilchrist ^{39/xi-14} finds that this drug provokes a profuse diuresis which relieves the overburdened ventricle in certain advanced forms of cardiac failure, notably in cases in which digitalis, dieting and the common diuretics have no effect in removing the œdema. The dose employed was generally 1 c.c. injected into some œdema-free area, either the buttock or the back. Subcutaneous injection must be avoided as the drug acts as an intense local irritant. It was noted that in two cases the results obtained were not those which would ordinarily be expected. In both of these cases the ventricle was completely exhausted. Further experience will be necessary in order to determine which type of heart patient will benefit from the treatment. It was noteworthy that in both unsuccessful cases the vital capacity was less than 30 per cent. and there was great venous engorgement. Gilchrist concludes that novasurol appears to be a most suitable adjuvant to digitalis therapy, and is apparently more reliable and more potent than any other diuretic at present in use. Owing to the presence of mercury in the drug its use would seem to be contra-indicated in the presence of renal disease.

PARATHYROID EXTRACTS

Our readers will recall that during the past year Prof. J. B. Collip, Head of the Department of Biochemistry of the University of Alberta, gave us his first clinical paper on his work of the internal secretion of the parathyroid glands. His technical paper appeared in

the *Journal of Biological Chemistry* (63:395). With the conviction that the parathyroid gland contains a hormone which, if obtained in potent form, could be used successfully in replacement therapy, an attempt was made to extract it. Parathyroid glands were removed from oxen at the time of slaughter, chilled and frozen at once, packed on ice and transported to the laboratory in an ice-box at 4° C. Glands were extracted with an equal volume of HCl and placed in a boiling-water bath for one hour, the glands began to disintegrate after a few minutes' heating. After the necessary period had elapsed the fat was removed from the surface mechanically. The extract was chilled to room temperature and made alkaline to pH 8 by NaOH. HCl was then added slowly until a maximal precipitation of protein and protein derivatives occurred. The precipitate was removed, redissolved in weak alkali and a second iso-electric precipitation carried out. The filtrates, or, if the centrifuge was used, the supernatant fluids, were combined, and this preparation represented an aqueous solution of the active principle. This form of preparation of the thyroid hormone could be administered by stomach, subcutaneously or intravenously. By the use of this extract parathyroid tetany can be prevented in parathyroidectomized dogs. The extract produces its effect by causing the calcium content of the blood serum to be restored within normal limits. A very close parallel has been observed between the clinical condition of the experimental animals and the calcium content of the blood serum. Overdosage effects have been observed and the blood findings in this condition invariably show a condition of hypercalcaemia, *i.e.*, anorexia, vomiting, apathy, drowsiness verging into coma, and a failing circulation. Hypercalcaemia in these animals is a fatal condition if allowed to persist. It has been found that sodium bicarbonate will reduce the calcium content of the blood serum in hypercalcaemia. With this extract tetania parathyreopriva has been prevented or controlled in dogs receiving no pre-operative preparation, and which have been placed on a heavy meat diet immediately following recovery from the operative procedure. On temporary withdrawal of the extract, tetany has supervened.

Collip, Clark and Stott ^{32/v.63:439} have found that in normal dogs this extract causes an elevation in level of the blood serum calcium, and the changes so produced follow a typical curve and the effect of

successive injections of the potent extract is to cause hypercalcaemia, which when long enough maintained may result in death.

PARATHYROID TETANY

C. L. Ogle ^{35/v-26} reports a case history of post-surgical parathyroid tetany, followed for twenty months, which for its value from the standpoint of the physiology and therapeutics of this gland, is inestimable. This case was very carefully reported and confirmed for a human the classical experiments on parathyroidectomized dogs, as recorded by Luckhardt and Dragsted. High protein diet, and low calcium intake both induced tetany, though the patient was able to tolerate a mixed diet plus calcium, long before a protein free one without it. During the early, desperate attacks of tetany, calcium chloride and lactate were both given by mouth and intravenously, accompanied by one-fifth of a grain of parathyroid and one grain of thyroid, without controlling the symptoms. At one time 220 c.c. of a 5 per cent. solution of calcium lactate were given before the tetany was controlled. It was not until the classical experiments of the parathyroidectomized dogs were recalled that an intake of calcium proportionate to the amount of the gland removed was tried. If the removal was total the patient would have had to take 1100 grains of calcium daily, she was given 100 grains every three hours, put on a protein free diet, colonic lavage and a 5 per cent. lactose rectal drip. This with the thyroid and parathyroid gland prevented the tetany. A gradual reduction of the calcium was attempted, and the tetany recurred, when the dose was 25 grains every four hours, for two days only. The author believed the gland extracts only exaggerated the diarrhoea and discontinued them when the danger of thyroid deficiency was found to be over. The similarity between the experimental and human tetany is striking—intestinal stasis, diet, calcium intake, and menstruation all having the same influence.

PARESIS

Malarial Treatment of.—G. B. Lake ^{47/iv-7} reviews the literature with reference to the treatment of paresis by malarial infection, which shows that 941 cases have been treated by this method. Of these 291, or 30.9 per cent., showed what were classified as complete remissions, most of these patients being able to return to their former occupations. This method of treating paresis rests, at the present

time, on a wholly empirical basis. The technic of the treatment presents no great difficulty in its performance. The only basis for the results reported seems to be connected with the hyperpyrexia produced by the malarial infection. No deaths were found recorded which were directly or wholly attributable to this method of treatment, though the malarial treatment may submit the patient to a possible danger of shortening his life. It seems that the attacks of inoculation malaria prove to be more readily and promptly controlled by quinine than is usual with spontaneous attacks. Cases with the most definite and complete clinical remissions frequently show little or no change in the spinal fluid findings; while a few cases in which the spinal fluid became completely negative showed no clinical improvement whatever. Other workers on this subject are finding that the continued mechanical transmission attenuates the fever-producing powers of the parasite. Fresh strains are needed to prevent this.

W. P. Larson and G. Fahr ^{41/vii} have shown that rabbits may be immunized against pneumococci treated with sodium ricinoleate and that the serum of such rabbits protects normal rabbits against intraperitoneal and intravenous pneumococcic infections. On the basis of this work a series of monkeys was treated with the serum and later a series of patients with pneumococcus pneumonia. The course of the disease under this treatment in seven cases is described. Of these cases two terminated fatally, but in every instance there was a fall in temperature and improvement, which in five of the seven cases progressed to complete recovery. Chills came on about one hour after the injection in three of the seven cases, and were accompanied by cyanosis and dyspnoea, which, however, was not of serious degree.

POLIOMYELITIS

Muscle Testing.—Dr. Richard Kovacs described before the recent New York meeting of the Electrotherapeutic Society, his methods of muscle testing and the application of physical therapy in the treatment of chronic poliomyelitis as applied at the Reconstruction Hospital in New York. Here 42 cases have been treated during the past four years; the earliest was of six months' and the oldest of eighteen years' standing. No case should be treated without a preliminary muscle test. The general plan of treatment includes an introductory treatment with radiant light for fifteen minutes; this

promotes local nutrition, improves skin conductivity and muscular response. If the muscle is only weak the faradic current is employed, using either the Bristow coil or high-tension faradic coil, with surging current. The technic consists of applying an indifferent electrode over the spine and a small active electrode (1 to 1½ inches in diameter) over the individual muscles. In muscles lacking faradic response the slow (galvanic) sinusoidal is the current of choice. Interrupted galvanism is used with the same technic as the sinusoidal, the active electrode being attached to the negative pole of the apparatus. Kovacs does not believe that the treatment of muscles *en masse*, that is, putting the same amount of current through all muscles, whether paralyzed or not, is as beneficial as the method of individual muscle stimulation. Reëducation should go on simultaneously with electric stimulation. Muscles responding to faradism, or up to 0.09 microfarad of the condenser set will recover voluntary power within a short period; with response under 0.90 on the condenser set, muscles will usually recover under appropriate electrical stimulation and adequate orthopædic support; muscles with condenser response of over 1 microfarad, or with response to strong interrupted galvanism, will require a long course of careful treatment, but present still a possibility for recovery. Muscles in which there is a total lack of response to any electrical stimulus may show a return of some electrical response, but the writer has never seen the return of voluntary power to such muscles. Electrical muscle stimulation can cause movements similar to the normal ones, even in degenerated muscles, and thus preserve the functional properties of the muscle until the normal nerve impulse returns to carry on the work. No case is too old for instituting proper electrotherapy. The earlier it is begun after the acute stage, the more satisfactory will be the results. Definite technic and persistency are the keynotes of success. Electrical treatment should always be an adjunct to indicated orthopædic measures.

PREGNANCY

The Value of the Leukocyte Count as an Aid in the Diagnosis of Ectopic Pregnancy.—In her observations on the leukocyte count in 150 cases of ectopic gestation, Lilian K. P. Farrar^{58/x1} finds that the leukocyte count fluctuates according to the amount of fresh blood being thrown into the peritoneal cavity and the rate of absorption. The leukocyte count tends to drop quickly to normal as the blood

in the peritoneal cavity is absorbed or walled in; 48 per cent. of the 150 cases showed a normal leukocyte count before operation was performed. In 29 cases of unruptured tubal pregnancy in which there was no free blood, and in 43 cases of ruptured pregnancy where the blood was walled in, the leukocyte count was normal. In this series of cases the leukocyte count was an index to the amount of free blood in the peritoneal cavity and the polymorphonuclear leukocyte count was increased markedly only in cases having fresh blood in the pelvis, and it increased in direct proportion to the amount of recent blood found at the time of operation. The fluctuating leukocyte count together with the moderate elevation of temperature differentiates gestation from a purulent salpingitis, with its more uniform high leukocyte count and fluctuating temperature. In cases of rupture of tubal pregnancy the steadily rising leukocyte count indicates active bleeding before the fall in the number of red cells or hemoglobin give warning of the condition. The leukocyte count to be of diagnostic value must be taken at least daily and in critical cases even hourly; it should be used in conjunction with the history and clinical findings in the case.

Seventeen cases of eclampsia, ante-, intra-, and post-partum treated by the intravenous use of magnesium sulphate, are reported by E. M. Lazard,^{3/11} with but one maternal death. In all instances the patients were profoundly toxic, having convulsions and being in coma when first seen, and most of them had had little or no antepartum care. The treatment consists of the intravenous injection of 20 c.c. of a 10 per cent. solution of magnesium sulphate as soon after the first observed convulsion as possible. In no case was the author unable to control the convulsions, apparently the only question being to get a sufficient amount of the solution into the circulation to accomplish this end. As a result of his experience, Lazard concludes that by the intravenous use of sufficient magnesium sulphate the convulsions of eclampsia can be controlled. This treatment reduces the œdema, promotes diuresis, and eliminates the toxins. Other eliminative measures, such as catharsis, phlebotomy, lavage, and colonic flushings may be used as adjuvants; the author has, however, gradually reduced this supplementary treatment until in the last two cases in his series, little else was done.

Non-syphilitic Diseases of the Fœtus.—E. Jeanselme and Paul Lefèvre^{54/xii-12} endeavor to show that miscarriage, intranatal mortality and a number of early infantile deaths are not always indubitable signs of syphilis. Although syphilis is unquestionably the most important cause of death of the fœtus and is responsible for innumerable deaths among the new-born, there are other morbid factors which bring about the same result. When one obtains a history of a number of miscarriages, intranatal deaths and early infantile deaths, a critical study of the patient should be made before concluding that these are the result of syphilis. The patient should be interrogated as to the cause of intranatal and infantile deaths. The author reports two cases in which the history with reference to miscarriage and still-births was suspicious of lues. In one of these it seems that the miscarriages were due to albuminuria; in the other case, two still-births were due to the cord being wound around the neck of the child, and in a third to prolonged labor and forceps delivery. The period of pregnancy at which miscarriage occurs is most important. If it occurs during the first three months, it is probably due to causes other than syphilis; if, on the other hand, miscarriage occurs during the fourth, fifth or sixth month, it is often due to syphilis. Premature births at the seventh and eighth months are rarely due to syphilis. The number of miscarriages is highly important, but it is still more important to note the duration of the respective pregnancies. If one finds a first pregnancy ending at four months, a second at six months, a third at eight months, and a fourth prolonged until term, this is almost a certain sign of the syphilitic origin of the miscarriages, unless there is a uterine malformation which has through successive miscarriages adapted itself to the carrying of a fœtus to term. The condition of the fœtus at the time of expulsion is significant with reference to syphilis. Since syphilis does not cause abortion but rather the death of the fœtus, a macerated fœtus is evidence of syphilis. A fact very carefully verified is that a placenta weighing more than 500 grams should immediately arouse suspicion of syphilis. With a placenta weighing more than 500 grams, the infant should not be given to a wet-nurse without first making a blood examination in both mother and child. Among causes of miscarriage and still-birth that must be kept in mind, before attributing them to syphilis, abor-

tion induced by either medicaments or instrumentally, and accidents during delivery.

The Early Diagnosis of Pregnancy by the Glycosuria-phloridzin Test.—Arthur Grunberg (*Journ. de Méd. de Paris*, 49:1031, Dec. 5, 1925) states that most of the tests suggested for the determination of the presence of pregnancy during the early months are extremely inconstant. He has made observations with the glycosuria-phloridzin test in 300 different subjects. This test consists of injecting 1 or 2 milligrams of phloridzin; in pregnant women this will provoke a glycosuria without hyperglycæmia. In the author's series of cases, the results show that this test gives a positive reaction during the first three months of pregnancy. It becomes rapidly negative after the development of the placenta. The reaction can be employed for the diagnosis of extra-uterine pregnancy. The author concludes that the glycosuria-phloridzin test is of the greatest value in the diagnosis of early pregnancy when other symptoms are non-existent or doubtful. A negative reaction excludes the possibility of pregnancy, while a positive reaction gives a probability of pregnancy of 80 to 90 per cent.

Severe Renal Symptoms.—Heynemann ^{63/x-10} points out that in making a differential diagnosis between eclampsia and uræmia during pregnancy the most essential factor is the estimation of the non-protein nitrogen, urea and indican of the blood. His observations on 73 cases of eclampsia confirm the findings of others that these substances are only slightly increased in eclampsia, while they are greatly increased in uræmia. He noted, however, that considerably increased percentages were often present shortly after eclamptic convulsions, in post-partum eclampsia and in the early puerperium. In these conditions percentages of 60 mg. per cent. do not rule out a diagnosis of eclampsia, but small percentages nevertheless favor that diagnosis. Findings suggestive of uræmia are an ammoniacal smell of the breath and an increased specific gravity of the urine, in spite of the greatly reduced total amount. Anuria may occur in either condition. The differential diagnosis of pregnancy nephropathy and chronic nephritis with severe symptoms in pregnancy is difficult. A considerable rise in blood-pressure, the finding of erythrocytes in the urine and albuminuric retinitis may be found in cases of pregnancy nephropathy, as well as in chronic neph-

ritis. When the renal signs appear in the latter months of pregnancy they favor the diagnosis of pregnancy nephropathy, unless chronic nephritis can be clearly demonstrated; confirmatory evidence is afforded if there is an antecedent history of eclampsia or pregnancy nephropathy, if the existing pregnancy is multiple or if the patient is primiparous. On the other hand, it is usually in the early months of pregnancy that acute renal symptoms develop in the presence of chronic nephritis. A diagnosis of pregnancy nephropathy is favored by the absence of hematuria and increase in blood-pressure. Hypertrophy of the left ventricle is suggestive, though by no means conclusive evidence of chronic nephritis. Renal symptoms in previous pregnancies point to pregnancy nephropathy.

Curietherapy of Cancer and Leiomyoma of the Uterus.—Gagey (*Gynéc. et Obstet.*, V. 12:357) gives the results of radium treatment at the Paris Radium Institute. Of 355 patients with cervical cancer treated up to the end of 1923 and followed up regularly, 100 (28 per cent.) appear to be absolutely free from cancer. The statistics in this series of cases confirm the statement made by M. Siredey and the author in 1921, *i.e.*, epidermoid epitheliomas (spinocellular) have supplied a larger number of cures than other epithelial cancers. In cancer of the cervix the use of radium followed by hysterectomy gives greater promise of cure than radium alone. It is better to apply radium before operation rather than after, but if the diagnosis has not been made before operation, there should be no hesitancy in making the application post-operatively; such an application, however, demands that greater precautions be taken. It is generally accepted that treatment of cancer of the body of the uterus is hysterectomy, and here there is no need of the pre-operative application of radium; in fact, such an application of radium is useless, provided one can remove the uterus by the abdominal route, without opening the uterine cavity and thus running the risk of disseminating neoplastic cells. If for one reason or another (age, size of the uterus, obesity, etc.) one chooses vaginal hysterectomy the conditions change. By this route one cannot remove the uterus without sectioning it; hence it is better to sterilize the uterus first by the use of radium. In 281 selected cases of fibroids treated during the period 1919–1924, there were ten failures; in other words, there were 96 per cent. of cures. The author again emphasizes the statement that the type of fibroid

suitable for curietherapy is that of small volume, not larger than the size of a three or four months' pregnancy, without complication, and principally the hemorrhagic type of fibroid.

Influence of Forceps on Infant Mortality.—G. Rittershaus ^{43/v:vi} reports that at the Freiburg Women's Clinic, among 17,942 deliveries 8.32 per cent. were forceps cases, with a total infant mortality of 0.378 per cent. He confirms Winkel's indications in the infant for the use of forceps, namely, heart sounds below 100 in a single pause between pains. From the standpoint of the mother, he considers extension of the second stage of labor beyond three hours, the necessary conditions being present, as a relative indication for forceps application in the interest of both mother and child. He concludes that forceps used under proper indications fulfill a benevolent purpose and favorably influence infant mortality.

PSICAINE

A. J. Copeland and E. Watson-Williams ^{19/i-3} separately report on the properties of an artificial cocaine called "psicaine," manufactured in Germany, where it is said to be twice as expensive as cocaine, to possess twice its anæsthetic power, to be only half as toxic, and not habit forming. These two investigators working independently disagree with these findings, considering it to have about the same or less anæsthetic power, to be about as toxic as cocaine, though the latter says that its claim as a non-habit forming drug is sound as the dose necessary to produce excitement is so large as to preclude it as a drug of this category. This is intensely important to the medical profession because if it can replace cocaine it will be a boon to humanity.

RADIUM

From experiments made by A. Kotzareff ^{56/vi-4} it is shown that the introduction into the circulation of radium emanation (alpha, beta and gamma rays), in maximum doses of 16.5 millicuries, produces no grave lesion in the organism. If there are no complicating factors, such as infection or repeated losses of blood from hemorrhage, no important modification can be found so far as the formed elements of the blood are concerned. The serum, on the other hand, seems to be modified electrocolloidally. It appears to contain new substances, or at least there is a new quantitative relation of its components, especially the elements of protein disintegration—albuminose, pep-

tones, amino-acids, etc. This modification persists for ten to twelve days after the injection, when there is a return to normal. The intramuscular injection produces the same effects. Local application produces necrosis. The waste products of necrotic cells circulate in the organism and poison it and then there are modifications of the formed elements, both as to their number and the leukocyte ratio. Briefly, there is radiodermatitis and hyperplasia, with serological modifications and modification of the blood tissues in general. The conclusion reached is that radium injections are without danger to the organism in general and for the blood tissue of the cancerous individual in particular. In the course of this investigation the author has obtained confirmation of the elective fixation of radium emanation on neoplastic and embryonic cells.

RAT-BITE FEVER

Th. Joekes^{39/xii-12} has been able to culture the *Spirillum morsus muris*, the etiological factor of rat-bite fever, to the thirty-fourth subculture. A motile coliform bacillus accompanies the spirillum as in the case of Kermorgant's spirochæte of mumps. The presence of yeast in the cultures apparently killed the spirilla within twenty-four hours.

RHEUMATIC FEVER

Homer F. Swift^{4/xi} considers this affection as a distinct disease entity, comparing it with tuberculosis and syphilis in its power to produce the symptoms of a general disease. This author has obtained autopsies, in cases that died in the first few weeks of the infection, none of which showed any gross lesions on the heart valves, though histologically there were numerous collections of leukocytes, lymphocytes, and large endothelial cells throughout these structures. These infiltrations were in the interstitial tissue, and not in relation to the contact edges of the valves. He considers that the verrucæ are due to the formation of thrombi upon necrotic areas, which appear over these infiltrations, because of interference with nutrition. This theory would indicate that the damages to the heart valves are not due to the presence of bacteria in the blood stream *per se*, but are secondary to some toxic deficiency of the internal blood supply. This idea also accounts for the common occurrence of vegetations at points other than contact edges. Ninety per cent. of these patients showed pathological electrocardiograms probably due to some selective action

on the heart-muscle, or its conduction system. This author discounts the importance of errors in diet and defects of metabolism, and advises the maintenance of a high nutritional level. He feels that salicylates and other anti-rheumatic drugs tend to mask symptoms, and that patients discharged while under their influence may have relapses. The period of rest is most important and should be lengthened, well beyond the period of infection. The average unit stay in hospital for seventy-two patients was 110 days.

This conception should alter our attitude toward the therapeutics of this disease. There has been a more or less common, but unfounded, belief that errors in diet or metabolism are important etiological factors in rheumatic fever. As a result of these opinions there has arisen the practice of omitting fruit and red meat and reducing the amount of carbohydrates. As a result of this course many patients suffer from under-nutrition with a consequent deleterious influence on their natural powers of resistance. In the writer's experience the maintenance of nutrition is one of the most important therapeutic measures for rheumatic fever. Analysis of a large series of charts of rheumatic fever patients presents unquestionable evidence that the drugs which have been considered as specific are probably merely anti-symptomatic in their action, and if patients are carefully studied while under their influence signs of persisting infection will be discovered. Many patients who have been allowed to be up and about in wards or in their homes, while under the influence of salicylates or neochinophin, have had relapses when these drugs were discontinued. It would seem that the practice of discharging patients from the hospital while under the influence of these drugs is a mistake. The period of rest needed is longer than is usually recognized or enforced. A summary of the length of time spent in the hospital by seventy-two patients with rheumatic fever showed an average of over 110 days and this did not include an average of two to six weeks in a convalescent home. In cases of rheumatic fever special care should be exercised to keep the patients quiet until signs of active infection have passed.

RICKETS

The Ultra-violet Rays in Rickets.—A great deal of attention was attracted about a year ago to the work of Dr. Alfred F. Hess showing the influence of ultra-violet rays in the prevention and treatment of

rickets. More recently this author ^{35/iv-4} presents a study of the conditions under which ultra-violet light is most effective. Strictly speaking, he says, the broad statement that ultra-violet radiations prevent or cure rickets is incorrect. In considering the ultra-violet rays of the sun, one must constantly bear in mind that there are marked diurnal and seasonal variations in this portion of the spectrum. The ultra-violet rays are weak in the early morning and in the evening and of the greatest intensity between the hours of 10 A.M. and 1 P.M. There is also a marked and important difference in the quality of the sunlight; radiations about 20 millimicrons shorter are furnished as the sun climbs from 10 to 60 degrees. These diurnal variations vary at different times of the year. The amount of radiation within what may be termed "the anti-rachitic region of the solar spectrum" is very small during the winter months. A comparison of the yearly amount of actual sunshine in the temperate zones demonstrates that there is no close parallelism between the incidence of rickets and annual sunshine. It shows, furthermore, that the occurrence of rickets does not depend on the equable distribution of sunshine throughout the year. The determining factor is the quality, not the quantity, of the sun's rays—the amount and intensity of those short ultra-violet radiations which alone are of value in preventing rickets. Hess has found the results of heliotherapy during the winter months disappointing, owing to the fact that "the anti-rachitic region of the solar spectrum" is very limited at this season and the infants cannot be exposed directly to the rays on account of the severity of the climate. It seems that the amount of effective solar radiations is so small in the winter that even if we substitute quartz panes for ordinary window glass, it will be insufficient to afford protection and eradicate rickets. The most promising prophylactic measures are ultra-violet light from artificial sources or the use of cod-liver oil or potent extracts of this oil. Certain experiments which Hess and others have carried out indicate that foods that have been activated by irradiation will prove to be of value in this connection; for example, dried milk that has been rendered anti-rachitic by this means. It is suggested that something may be accomplished by improved hygienic conditions of milch cows. At present many of those that furnish the best grade of milk are kept throughout the year in sunless barns, are

allowed a very limited amount of exercise, and receive little or no fresh green fodder.

The experiments of Harry Steenbock and Amy L. Daniels,^{35/iv} carried out to show the effect of ultra-violet radiation in a variety of foodstuffs, demonstrated that, by exposing such foods as wheat, shredded wheat biscuits, corn flakes, patent wheat flour, cornstarch, meat, milk and egg-yolk to ultra-violet light, they can be endowed with rickets-preventing properties. That such a wide variety of foods can be affected appears to be due to the fact that practically all naturally occurring foods contain lipoidal constituents of the nature of sterols which can carry this activation. Cholesterol, for example, as obtained from the brain, is entirely inactive, but after exposure to ultra-violet light becomes rickets-preventing. As fats are good solvents, practically all fresh fats can be activated, often to a degree to make them compare favorably with cod-liver oil. These authors point out that as anti-rachitic action consists of the induction of calcium assimilation and its conservation for the animal, this is a matter which concerns not only the young but also the adult.

More recently C. E. Bloch and Frans Faber,^{2/x} of Copenhagen, carried out experiments in which they determined the phosphorus and calcium content of the blood in about fifty children, all of whom exhibited the characteristic signs of rickets or tetany, or who had both diseases at the same time. In agreement with all previous work it was found that the blood phosphorus became normal under the influence of the quartz lamp. This effect in the present cases occurred within a month after a total exposure of one hundred minutes. These investigations showed that it was the light alone which caused the phosphorus to rise, and, as it remains present in normal amount even when the exposure is discontinued after a few times, this stable condition cannot be due to the fact that the light has contributed or liberated a missing substance, be it phosphorus or a vitamin, because these bodies are constantly used up during growth, and a new supply must therefore constantly be furnished. It is more likely that a depressed function is revived by the action of light. The ultra-violet light acts on tetany just as it does on rickets. The blood calcium remains normal even if the exposure to the rays is discontinued. These authors also argue that as cod-liver oil has the same healing action on rickets and tetany as light has, and that as this effect is not

due to vitamin A substance, there must be a stimulating factor in cod-liver oil similar to that in ultra-violet light in addition to the vitamin A substance, and that the non-specific stimulating factor must be the violet rays. Evidently, in the opinion of these authors, the hypothetic vitamin does not exist.

SEASICKNESS

According to a paper covering the wide experiences of P. H. Desnoes^{35/1-30-1926} seasickness in the healthy adult is usually due to an excessive stimulation of the labyrinth. Its effect on the body as a whole may be explained by radiation of these stimuli from their receptive centre in the brain to other associated centres, as the vasomotor, respiratory and vagus. Eye-muscle fatigue, muscle-sense disturbance, reflex irritation from the gastro-intestinal tract, and neurotic or psychic reactions in certain types of individuals may also be factors entering into the problem. In treatment Desnoes places his main reliance on scopolamine hydrobromide given in small, but frequently repeated, doses of 1/400 grain combined with strychnine if there be much depression. In addition chlorbutanol or some other centrally acting sedative hypnotic such as sodium barbital, phenobarbital, sulphonethylmethane or suphonemethane will be found useful. Cocaine is not to be recommended. The practice of taking a deep inspiration as the ship descends, thus "splinting" the abdominal viscera, and releasing the breath after the vessel has risen, has been used with asserted success by Wollaston. In combating the contributory factors, attention must be given to proper diet and bowel elimination.

THROMBO-ANGIITIS OBLITERANS

Herman B. Philips and Isidor S. Tunick^{35/v-16} present a preliminary report on the results of röntgen-ray therapy in a series of 50 cases of circulatory disturbances of the extremities, most of which were thrombo-angiitis obliterans. The doses of röntgen-rays are essentially stimulating ones, and consist of from ten to fifteen minutes' exposure alternating at weekly intervals over the mid-anterior and posterior aspects of the body, from the tenth dorsal to the fifth lumbar vertebra in lower extremity affections, and over the cervical and upper two dorsal segments in upper extremity disturbances. The following factors were used: 5 milliamperes, 100,000 volts, 5-mm. aluminum

filter, 15-inch distance. The relief of pain usually occurred in two or three weeks' time after the inception of the treatment, although immediate relief was obtained several times. Relief is progressive and fairly uniform, the exceptions being less than 10 per cent. With relief of this symptom nature and time heal most of the lesions. There was pronounced improvement in the intermittent claudication within one or two weeks, so that the patient could walk without distress for considerably longer distances. This disturbing symptom disappeared completely in 50 per cent. of the cases, after the sixth week, with very material relief from this distressing symptom in all. Improvement in the circulatory and trophic disturbances is noticeable in from one month to six weeks. There is a distinct change in the color of the extremity, the cyanosis or rubor disappearing. The limbs become warmer and the patients are better able to withstand changes of temperature. No restoration of absent pulses was noted at any time nor in any of the cases, nor is it possible to state with positiveness that improvement in the pulse was noted in any instance. The favorable changes in the circulation are attributed to improvement in the collateral circulation as well as to diminution of the venous obstruction.

Another form of treatment which has been applied in cases of thrombo-angiitis, ulcer of the leg and gangrene of the toes is that of periarterial sympathectomy, which is described by Balfour and Reid on page 292 of this issue. Leonardo Dominici ^{52/1-5} warns that the early results of periarterial sympathectomy are not a sufficient criterion of the success of this operation.

SPLEEN See ANAPHYLAXIS

SEDIMENTATION TEST See BLOOD

STOMACH

The Excretion of Neutral Red in the Human Stomach as a Functional Test.—Asher Winkelstein and Joseph M. Marcus ^{24/x-31} review the application of chromoscopy to the study of the secretory function of the stomach, and because of the comparative novelty of the subject and the conflicting views given in the literature as to the value of these dyestuff tests they have studied a series of forty-six unselected ambulatory patients in the gastro-intestinal division of Mount Sinai Hospital, New York. The technic employed was this:

The patient comes with a fasting stomach, the Rehfuß tube is passed, and 2 c.c. of a 1 per cent. solution of neutral red (Ehrlich's neutral red freshly dissolved in distilled water and boiled) was injected intramuscularly in the gluteal region. The gastric contents were aspirated every two minutes until the dye appeared as a definite pink discoloration. If no dye appeared the aspiration was continued for two hours. The acidity figures were confirmed by the Rehfuß, Ewald, alcohol and meat extract test meals. Patients with normal or subnormal free hydrochloric acid figures excrete the dye in a fairly constant average time of twenty-one minutes. In hyperacidity the appearance of the dye is hastened to seventeen minutes. Patients with duodenal ulcer or gall-bladder disease, with or without hyperacidity, often show a similar figure. In achylia gastrica, the excretion time is greatly prolonged to an hour or more. In most cases the dye does not appear in the stomach. These authors think the test may prove of value, in addition to the usual methods, in the study of the secretory function of the stomach, particularly in the various forms of achlorhydria and achylia gastrica.

A somewhat different view is expressed in an article by Percy B. Davidson, Edouard Willcox and Cushman D. Hagensen,^{35/ix-12} who find that the appearance time of neutral red in the stomach after the intramuscular injection is not sufficiently uniform in various gastric syndromes to be of clinical value. The presence or absence of excretion of the dye are the only points of clinical significance, *i.e.*, in the differentiation of two types of gastric anacidity, those who do and those who do not excrete dye within the two-hour test period. In the former group are cases of carcinoma of the stomach and those of secondary anæmia with anacidity; in the latter group are the cases of pernicious anæmia and one doubtful case. There were several cases in which the differential diagnosis between secondary anæmia with anacidity and pernicious anæmia has been difficult; the differentiation by the excretion of neutral red has been very helpful in these instances. It seems probable that the excretion of neutral red in the human stomach is dependent upon the presence of hydrochloric acid secretory tissue.

TETRA-ETHYL LEAD

A. Hamilton *et al.*,^{35/v-16} reviewing the reports in the literature, on the toxicity of lead halogen compounds in gasolene, both from the

standpoint of its manufacture and its consumption, conclude that it constitutes a public danger in both instances. These authors criticize the report of the Bureau of Mines which practically exonerates this compound as used in gasolene, and quote others in this criticism who claim that the experiments were inadequate in numbers of animals and in controls. It appears that chlorides, bromides, sulphates, oxides and metallic lead fine enough to float as lead dust, occur in the exhaust gases of engines burning this substance. The careless handling of the compound in its manufacture is shown to be highly dangerous, though improvements in the manufacturing apparatus have reduced these dangers. These writers conclude that the use of ethyl gasolene affords a real danger of chronic lead poisoning amongst garage workers and employees of gas-filling stations, and that there is a possible danger to the public from the lead dust thrown out from the exhausts of motors in large cities. They claim that in the manufacture of this compound, the danger is greater because of its absorption through the skin. The danger to the public from the lead in exhaust gases is magnified by the fact that some of the compounds are soluble salts. They earnestly urge the more complete investigation of a problem so vast and important as this is to the public health.

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RECENT PROGRESS IN SURGERY

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TOXÆMIA ASSOCIATED WITH GASTRIC STASIS

THE results of gastric surgery have been notably improved since the recognition of chemical changes in the blood, associated with pyloric obstruction, benign or malignant, and the introduction of therapeutic measures to control them. The clinical manifestations associated with these chemical changes are: Vomiting, dehydration, neuromuscular irritability, prostration, low blood-pressure, and oliguria or anuria, and in severe cases delirium resembling that of typhoid fever. Advanced chemical changes in the blood are coincident with the poor general condition of the patient. When these are recognized and corrected, his condition improves and the risk of operation is less.

If such toxæmia exists, the diagnostic criteria are:²¹ (1) Increase in the blood-urea, (2) decrease in the plasma chlorides, and (3) a tendency toward increase in the alkali reserve of the blood, as shown by an increased ability of the plasma to combine with carbon dioxide. Slight chemical changes occur without any clinical evidence beyond gastric retention. The blood-urea is usually the first to show change.

In the treatment of this condition ³¹ intravenous injections of 10 gm. of a 1 per cent. solution of sodium chloride and 100 gm. of a 10 per cent. solution of glucose in 1000 c.c. of freshly distilled water are given from one to three times a day, according to the severity of the toxæmia or the degree of chemical change in the blood. Twenty minutes are usually allowed for each injection. The sodium chloride and glucose strongly stimulate the urinary output, as well as peristalsis, and the body fluids are maintained. The chemical state of the blood will rapidly return to normal and can be maintained there

by the same measures. The same condition may occur post-operatively when there is a temporary obstruction due to a paralytic ileus or some other cause. In such cases the signs suggesting the toxæmia are: Falling blood-pressure, falling urinary output, and a negative fluid balance recognizable by comparing the gastric intake with the amount removed by lavage and emesis. The chemical changes in the blood and the treatment required are identical with those in cases of pyloric obstruction. Gastric lavage is employed only to remove excess, and to obtain diagnostic evidence. With the return of the blood to a normal condition and its maintenance there, an obstruction that is not organic will usually be relieved. If it is not relieved it is probable that the obstruction is organic and requires surgical intervention.

Toxæmia of this type must be distinguished from that of nephritis in which the blood-urea is increased, the chlorides increased, and the carbon dioxide combining power of the plasma decreased.

In those cases of pyloric obstruction without toxæmia, the administration of fluids by rectum, hypodermic injection, and by mouth, and the institution of regular gastric lavage to insure having the stomach clean at operation, facilitate surgical treatment and add much to its safety, particularly if the obstruction is due to carcinoma.

THE DEVINE OPERATION FOR DUODENAL ULCER

In the surgical treatment of duodenal ulcer without obstruction, Devine introduced a procedure which consists of cutting across the stomach, excluding the distal part and joining the proximal part to the side of the jejunum behind the transverse colon, thus performing a Polya operation without removing any part of the stomach. He reports good results in all but three of a series of thirty cases. In two of the unsuccessful cases jejunal ulcer developed. In the third there was persisting melena, which, however, disappeared later. He found that the more he advanced the line of exclusion toward the fundus, away from the pylorus, the more rapid was the emptying of the stomach, the lower was the concentration of free acids after operation, and the better the result. He thus advocates an operation which is simple in technic, giving the same results as partial gastrectomy, but without the mutilation incident to it. It must not be employed if there is any pyloric obstruction.

EXPERIMENTAL PEPTIC ULCER

Mann and Williamson have been able to produce experimentally in dogs chronic peptic ulcers having the same characteristics as those in man. The method is summarized by Mann as follows: "The pylorus is sectioned and the distal end closed. The first portion of the jejunum is sectioned and the distal end anastomosed to the pyloric end of the stomach. The proximal end of the jejunum is drained into the ileum at a distance greater than 50 cm. from the pyloric anastomosis." The ulcer begins to form approximately one month after the operation and occurs in the jejunum just distal to the anastomosis with the stomach at a point described as "that where the acid gastric contents strike first and with greatest force on the jejunal mucosa," which is accustomed to an alkaline content, and it may spread to include the line of suture. The ulcers have the tendency to develop and to perforate as similar ulcers in man. They will heal if protected from the gastric content.

There is suggested in this experiment a mechanical and chemical explanation for the production of jejunal ulcers, or at least for their chronicity, and also for the chronicity of peptic ulcer in man.

TOTAL REMOVAL OF TUMORS AT THE CEREBELLOPONTILE ANGLE

A notable contribution to brain surgery has been made by Dandy. He has recently reviewed the difficulties and progress in the treatment of brain tumors, especially with regard to cerebellopontile tumors. The results in these cases have been very disappointing since a high percentage of immediate operative deaths has followed all procedures, and since, chiefly because of lack of exposure, the tumor could not be removed *in toto*. Dandy describes a method of exposing and removing the tumor at the cerebellopontile angle together with its capsule, and he reports a series of cases.

The method of approach is by bilateral cerebellar decompression, and by enlarging the opening in the skull on the side of the tumor as far as the transverse and lateral sinuses will permit. The dura is incised and retraction of the cerebellum exposes the tumor. Its capsule is incised and the body of the tumor removed piecemeal by curette, as described by Cushing. The capsule is then carefully dissected out, particular attention being paid to hemostasis. The procedure is tedious, occupying as much as three or four hours, but the

results thus far have justified it, the mortality being less than for simple cerebellar decompression, partial removal, or removal without the capsule. The prospect for permanent cure is excellent.

OPERATIONS FOR ANGINA PECTORIS

Brown and Coffey, Kerr, Reid and Andrus report cases of angina pectoris in which parts of the cervical sympathetic system were severed and removed. This is done in an attempt merely to relieve the patients of their distressing pain, and has no influence on the etiologic factor of the disease.

The pain is thought to be caused by a spasm of the base of the aorta. This spasm affects the coronary arteries and, unless it is promptly relieved, the heart is deprived of sufficient blood supply, and death follows. If this spasm could be prevented by interruption of the reflex arc at the base of the aorta, the pains would stop. Attempts to accomplish this object have been made by division or removal of a part or the whole of the cervical portion of the sympathetic system, and division of the depressor fibres of the vagus.

Brown and Coffey suggested division of the superior cardiac nerve of the left side, a large branch from the superior cervical ganglion. If, following this procedure, there should be recurrence of the pain, they then advocated removal of the ganglion itself. The latter has been the operation of choice in all attempts to relieve the pains of angina pectoris. If relief is not afforded by this means, the surgeon can resort to more extensive dissections of the sympathetic chain, and division of the depressor nerve, which, however, is difficult to isolate in man.

From all types of operation the percentage of patients who have obtained relief has been reported as about the same, 80 per cent. The total failures are few. Death, apparently from heart failure or mild recurrences of the pain soon after operation, occurs in 8 per cent. of the cases.²⁵

OPERATION FOR RAYNAUD'S DISEASE AND ASSOCIATED CONDITIONS

In surgery of the sympathetic nervous system a somewhat similar procedure is the periarterial sympathectomy suggested by Jaboulay, brought forward by Leriche,²⁷ and recently reviewed by Bernheim with case reports. It is indicated in vascular disorders of the ex-

tremities that depend on a spasmodic condition of the blood-vessels, of which the clinical type is Raynaud's disease. Bernheim suggests that thrombo-angiitis, endarteritis obliterans, and Raynaud's disease may be different manifestations of the same process. The operation should be performed early in the course of the disease before signs of gangrene are apparent, but improvement even in such cases is reported.

The femoral artery is exposed in Scarpa's triangle, or the brachial just below the axilla in the arm, for about 5 cm., the sheath incised and the vessel denuded of its adventitia which may come off in one or more layers. The sympathetic fibres to the artery run in this coat and so are severed. The procedure, if successful, results in cessation of the spasm of the arteries and improved circulation to the extremity.

Various degrees of success are reported which may depend on the completeness with which the adventitial coat is removed. It is not established, however, that some failures may not be due to innervation by sympathetic fibres which go to the extremities with the spinal nerves and are given off to the artery at a point lower than that from which the adventitia is removed, as demonstrated by Potts.

In the hands of Cohen, who has reported a series of eleven cases, the best results have been obtained in cases of pain due to arteriosclerotic diseases of the vessels of the leg.

PNEUMONOGRAPHY AN AID TO DIAGNOSIS

Pneumonography was first introduced by Jackson in 1905, in an investigation of certain lung conditions. He used the insufflation of dry bismuth oxide without any harmful effects. Since then much experimentation has been carried on in the attempt to find the most suitable substances. This work has been summarized by Clerf, who concludes that the most suitable are dry bismuth subcarbonate and lipiodol.^{7, 8} The latter was introduced for this purpose by Sargent and Cottenot, and is a vegetable oil containing 40 per cent. of iodine by weight. With its use cases of acute iodism have been reported. Several days will elapse before it entirely disappears from the lungs. No deleterious effects are reported after the use of bismuth subcarbonate powder, and it is evacuated from the lung by coughing and ciliary action within forty-eight hours.

In examining the bronchus, which is exposed through a bronchoscope, the material opaque to the röntgen-ray is introduced directly

through a bronchoscopic insufflator. Of the lipiodol as much as 25 c.c. may be used in an adult, of the bismuth subcarbonate as much as 30 c.c. Stereograms of the chest are then taken.

The thoracic surgeon is afforded invaluable information since the method can be used for the following purposes: (1) Location of foreign bodies, (2) mapping of lung abscesses, (3) mapping the extent and degree of bronchiectasis, (4) location of bronchopleural fistulas, and (5) determination of the extent of malignant growths.

OPERATION FOR MITRAL STENOSIS

Cutler, Levine and Beck have developed a technic and devised an instrument whereby the mitral orifice may be enlarged in cases of mitral stenosis. They have performed this operation on four patients; one was very much improved and still living one year after operation; the other three survived the operation ten hours, twenty hours, and six days, respectively. The last patient died from bilateral, post-operative bronchopneumonia. They justly point out that this mortality is not excessively high when compared with the results from the first attempts in many other branches of surgery.

In reporting these four cases, the authors give a very comprehensive review of the history of cardiac surgery, both on human subjects and experimentally on animals, and a detailed description of the experiments leading up to their attempts to relieve stenosis of the mitral valve.

The first attempts in cardiac surgery were made in cases of wounds. In 1897, Rehn reported the first successful case. In 1920, Tuffier reported a series of 305 cases with recovery in 50.4 per cent., as compared with about 10 per cent. in cases of untreated injuries. In 1902, Brauer proposed the operation of cardiolysis in cases of adherent pericardium, and reported successful results. In 1912, Tuffier operated on a young man with marked aortic stenosis, dilating the valve with his finger. The patient was living in 1920. Cutler, Levine and Beck have made the first surgical attempts to relieve mitral stenosis.

In experimental work the heart valves have been approached operatively through the ventricles, auricles, and large vessels, and defects made in them by knives and hooks. After the large vessels were clamped off, the valves have been approached directly and in-

spected. This method gave very little time for the performance of any operative procedure. Allen and Graham, in 1922, devised a cardioscope equipped with a small knife which enabled them to cut normal valves under vision. Attempts were made experimentally to produce stenosis of the valves by ligatures and by contraction after exposure to radium. Methods of anæsthesia were devised to permit operation with the thorax open.

In reporting their own experiments, Cutler, Levine and Beck stated that the heart can withstand considerable trauma and recover normally. They gave up attempts to expose the valves directly by clamping off the circulation and concluded that the mitral valve is best reached through the left ventricle. They do not think the cardioscope practicable.

After the first attempts on human subjects they came to the conclusion that merely cutting the stenosed valve with a knife was not sufficient, and so devised their cardiovalvulotome, with which a piece may be bitten out of the valve and removed from the heart. This instrument was used in their last cases.

The anæsthetic which was used in all cases was ether, given by the Connell apparatus. The method of approach to the heart was through an incision in the median line, the sternum being divided longitudinally, and the linea alba incised for about 7.5 cm.; by means of an incision through the pericardium and diaphragm and by lateral retraction, the whole heart was exposed. The apex of the heart could be lifted to the right and held by a traction suture, and the left ventricle thus exposed. The incision in the ventricle was made near the apex and the instrument for cutting the valve inserted through two control sutures. When this was withdrawn, hemorrhage was controlled by one or two stitches. The pericardium and diaphragm were closed with silk, and the halves of the sternum held together by silver wire.

Great care must be taken in the diagnosis of mitral stenosis. Of greatest importance in this connection are the diastolic murmur with or without a thrill at the apex, and the presence of a prominent left auricle, as indicated by the röntgen-ray and changes in the electrocardiogram.

For operation, only those cases should be accepted in which the age of susceptibility to repeated rheumatic infection has been passed,

in which the heart-muscle is in good condition, and in which the mechanical obstruction is a marked feature.

RÖNTGENOLOGIC DIAGNOSIS OF DISEASES OF THE GALL-BLADDER

If a substance opaque to the röntgen-ray would be excreted by the liver into the bile and hence into the gall-bladder, a shadow would be obtained which would permit accurate inspection of that viscus. It would be necessary that the function of the liver be good enough to excrete the substance, that the cystic duct be open, and that the concentrating function of the gall-bladder suffice for the concentration in it necessary to produce the shadow.

With this as a foundation Graham and Cole first obtained a shadow of the gall-bladder by the intravenous injection of the calcium salt of tetrachlorphenolphthalein. They have since experimented with several substances and methods of administration, intravenously, subcutaneously, and by mouth and rectum.^{18, 19, 20} Their most satisfactory results have been obtained by the intravenous injection of the sodium salt of tetrabromphenolphthalein.

The preparation of the solution consists of dissolving 5 gm. of this salt in from 35 to 40 c.c. of freshly distilled water. It is then filtered and sterilized in a boiling water bath for from fifteen to twenty minutes. A dose of this proportion is sufficient in patients weighing 125 pounds or more, but should be reduced for those weighing less. It is given intravenously in two doses, at 7:30 and 9:00 A.M., care being taken that none is extravasated on account of the danger of tissue necrosis. The following directions for the patient should be carried out: (1) Breakfast is omitted on the day of the test; (2) lunch is omitted (a glass of milk being allowed); (3) no protein is allowed in the evening meal; (4) sodium bicarbonate is administered, 2 gm. every three hours while the patient is awake, for forty-eight hours; (5) water by mouth may be allowed, and (6) the patient should lie on the right side. Röntgenograms are taken four, eight, twenty-four, and thirty-two hours after completion of the administration.

Certain toxic symptoms may manifest themselves, such as nausea, vomiting, dizziness of short duration, and fall in blood-pressure. In most patients these are very slight and of short duration. When there is a fall in blood-pressure prompt relief follows the intramus-

cular injection of epinephrin. The best shadows are obtained in the normal gall-bladder, and failure of a shadow to appear would denote disease of the biliary tract, including the gall-bladder.

Whittaker and Milliken by experimental and clinical evidence conclude that, on account of its greater atomic weight, sodium tetraiodophenolphthalein is preferable to the bromine compound. They believe that the toxicity of the two drugs is about the same but that only half as much of the iodine compound is necessary to produce a shadow of the gall-bladder.

Their method is to use 0.04 gm. of the sodium tetraiodophenolphthalein for each kilogram of body-weight. This amount of the salt is dissolved in sufficient distilled water to make a 10 per cent. solution, to which is added from 1.5 to 2.0 c.c. of a 10 per cent. solution of sodium bicarbonate for the purpose of keeping the salt in solution. This is filtered, autoclaved at 15 pounds' pressure for thirty minutes, and kept sealed in a dark place. The injection is made intravenously by gravity at low pressure and at one sitting. The directions to the patient are similar to those given by Graham and Cole. Röntgenograms are taken at six, nine, twelve, twenty-four, and thirty-six hours. One-half hour before the first picture is taken, a soapsuds enema is given and a rectal tube inserted to relieve gaseous distention. After the nine-hour film, toast and cocoa are given to see whether food will cause any shrinking of the shadow.

The toxic symptoms are the same as those following the administration of tetrabromphenolphthalein and they are treated in the same way. Whittaker and Milliken had only four patients in a series of forty who showed reaction.

The conditions indicating disease in the gall-bladder are: (1) Failure of a shadow to appear, due to obstruction of the cystic duct or to severe chronic cholecystitis; (2) the appearance of gall-stones, which, although not seen in plain films, will show as negative shadows in the cholecystogram; (3) failure of the normal expansion and contraction of the gall-bladder, and (4) distortion of the shadow due to causes in or around the gall-bladder.

Whittaker, Milliken and Vogt also report on the oral administration of sodium tetraiodophenolphthalein for the same purpose. The patient is given 5-grain salol-coated pills to the amount of 0.08 gm. for each kilogram of body-weight. Starting at 8:00 or 9:00 P.M.

he takes one such pill every fifteen minutes with half a glass of water until the required dose is taken. The patient is directed to lie on his right side. Röntgenograms taken at twelve and fifteen hours will then show shadows of the gall-bladder but not as constantly as after the intravenous administration of the drug. Following the fifteen-hour film a meal is given the patient in order to bring out any change in the size of the cholecystic shadow. The effect on the patient is much less noticeable by this method and it is more convenient for both patient and physician. The shadows, however, are not as dependable as those obtained by the intravenous method, but cystograms are obtainable in 93 per cent. of normal subjects. Whittaker, Milliken and Vogt recommend the use of the oral method first, and then, if there should be any question as to the conclusiveness of the results, the intravenous method should be used.

Carman has used these methods of obtaining cholecystograms extensively and has reached the same conclusions as Milliken and Whittaker. He recommends the use of the bromine salt by mouth first, and the iodine salt intravenously to check doubtful conclusions.

THE VAN DEN BERGH REACTION FOR BILIRUBIN IN THE BLOOD SERUM ³⁰

The presence and degree of jaundice has, until recently, been determined by examination of the color of the skin and mucous membranes and by the presence or absence of bile pigment in the urine and fæces. These methods have been augmented by the addition of the van den Bergh test for bilirubin in the blood serum.

The test depends on the diazo reaction of Ehrlich, whereby a small amount of a diazonium salt in acid solution is added to an alcoholic solution of bilirubin with the production of an azo dye. With regard to icteric blood serum van den Bergh found that: (1) Some serums, by direct addition of the diazo reagent in the absence of alcohol, gave an immediate reaction within thirty seconds; this depends on some change which the bilirubin undergoes in passing through the bile capillaries and is therefore present in obstructive jaundice; (2) some serums, by the direct addition of the diazo reagent, gave no reaction or one only after standing for some time; this is the negative or direct delayed reaction and occurs when the bilirubin has not passed through the capillaries of the bile, and is present in hemolytic jaundice; and (3) the alcoholic extract of all

icteric serums gave an immediate reaction on addition of the diazo reagent; this is Ehrlich's original reaction for bilirubin and is van den Bergh's indirect reaction; it is used as a quantitative reaction, the amount of bilirubin present being determined by comparison with standard solutions.

To these has been added, by Feigl and Querner, the biphasic reaction in which, on the addition of the diazo reagent directly to the serum, there is a slight direct reaction followed by a gradual increase in the depth of the color. It depends on the presence of bilirubin which has passed through the bile capillaries and also on that which has not passed through the capillaries. It occurs in toxic and infectious types of jaundice.

The indirect reaction is very sensitive, being positive in dilutions of 1:1,500,000. Van den Bergh's unit is the amount of bilirubin present sufficient to make a concentration of 1:200,000. Normal blood serum always contains small amounts of bilirubin which is estimated at from 0.2 to 0.6 unit, with an average of 0.3 unit.

In cases of obstructive jaundice this amount may increase up to 4 units, or, roughly, ten times normal without the typical appearance of a jaundiced skin or mucous membrane or the presence of bilirubin, thus giving rise to the condition which is termed "latent jaundice." A patient, therefore, with surgical obstruction of the bile passages, although not actually jaundiced, may have blood changes which would place him in the same group with actually jaundiced patients. Also, by the recognition of the latent jaundice and by the successive estimations of the amount of bilirubin in the serum, it may be determined absolutely whether the jaundice in a given case is increasing or decreasing; the surgeon is placed on guard as to the necessary pre-operative treatment and is able to choose the optimal time for operation.

PREPARATION OF JAUNDICED PATIENTS FOR OPERATION

Lee and Vincent in a study of the coagulation time of the blood in cases of obstructive jaundice demonstrated a close parallelism between this and the tendency to hemorrhage, especially as seen at the time of operation. The presence of bile in the blood delays its coagulation, and this effect is largely counteracted by the administration of calcium. Calcium by oral administration must be given for a

period of several days before there is any marked change, but the authors demonstrated in dogs a prompt effect by the intravenous injection of calcium salts, and that the calcium could apparently be given in this way without bad results.

In the preparation of patients with obstructive jaundice for operation, Walters has used calcium chloride intravenously, and reports improvement in results,^{40, 41} especially with regard to post-operative hemorrhage, and he and Bowler have demonstrated that there are no deleterious effects from this method. In patients not so prepared, the cause of death following operation was found to be hemorrhage in more than half the cases, and in 73 per cent. of these the coagulation time of the blood was more than nine minutes. Hemorrhage was the cause of death in only 6 per cent. of patients with jaundice who died following operation.

The method is to give intravenously, slowly, 5 c.c. of a 10 per cent. solution of calcium chloride in distilled water daily for three successive days, and to force carbohydrates, especially glucose. The coagulation time is then estimated and if there is not a satisfactory reduction, the course may be repeated. A patient is not operated on until the coagulation time falls below nine minutes.

The cases of thirty-four patients thus prepared are reported, none of whom died from hemorrhage, and in only two did any bleeding occur from the wound following operation. In one of these the bleeding stopped immediately after the transfusion of citrated blood. No deleterious effect of the treatment occurred.

ANÆSTHESIA

In producing anæsthesia, when carbon dioxide is added to the inspired gas in a respiratory apparatus there is a certain response. In the majority of persons this is first an increase in the depth of respirations with a concentration of carbon dioxide as high as from 4 to 6 per cent., followed by an increase in rate.^{13, 23} By the addition of carbon dioxide to ether vapor, anæsthesia is also produced by lower concentrations of ether, and at the termination of the anæsthesia the carbon dioxide hastens the elimination of the ether.²² These effects of carbon dioxide are being made use of in the production, maintenance, and termination of anæsthesia by nitrous oxide, ethylene, ether and oxygen, and their combinations. Lundy reports a large

series of cases in which anæsthesia was thus carried out, a control for carbon dioxide being added to the gas machine.

Anæsthesia is induced by a mixture of nitrous oxide and oxygen to which carbon dioxide is gradually added until the respirations are doubled in depth. The concentration never exceeds 5 per cent. Ethylene is then used to replace the nitrous oxide slowly until a mixture is obtained of ethylene 75 per cent. ; oxygen 20 per cent. ; and carbon dioxide 5 per cent. The carbon dioxide stimulates deeper breathing, consequently the second, or excitement, stage of the anæsthesia is passed through with the elimination of the tendency toward respiratory inhibition. If greater relaxation is required during the operation for exposure, or for the closure of an abdominal wound, ether vapor may be added ; with the use of carbon dioxide, less ether is required for this purpose. If the abdominal wall has been previously blocked with novocaine the addition of ether to the anæsthetic during the closure is often unnecessary. Toward the termination of the operation the ethylene and ether are gradually replaced by nitrous oxides so that, by the time the skin sutures are in, most of the former are eliminated and the patient may often be awake before leaving the operating table.

In obstetrical practice the addition of carbon dioxide to the anæsthetic tends to prevent the excessive holding of the breath and bearing down which occurs when the head is against the perineum. In resuscitating the new-born infant carbon dioxide is also a very effective stimulant to respiration.

Lundy enumerates the advantages of using carbon dioxide in anæsthesia as follows: (1) Increase in rate of the absorption of ether, when used alone or with other anæsthetic agents, by increasing the volume of respiration; (2) low concentration of ether vapor; (3) reduction of struggling, breath holding, and shallow breathing, and the absence of cyanosis; (4) greater relaxation in light anæsthesia; (5) quieting effect of morphine without its occasional bad effects on the respiratory centre; (6) starting of respiration in new-born infants with the usual manipulations, if the air passages are clear; (7) better prognosis if patients are moribund from operative procedures or for other reasons; (8) lack of idiosyncrasy to low concentration; (9) safer induction and maintenance of gas anæsthesia, and (10) hastening revival of the patient and the elimination of ether.

If carbon dioxide is used in too strong a concentration over too long a period the symptoms are: Coughing, holding of the breath, and over-vigorous thoracic and abdominal movements, whereas if it is added in proper strength, it is expected that these symptoms will be obviated.

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CUMULATIVE INDEX

(THIRTY-SIXTH SERIES—1926)

(The Roman numeral refers to volume I, March.)

A

- Abduction, definition of, i, 76
- Adduction, definition of, i, 76
- Abscess, diagnosis and treatment of acute superficial circumscribed, i, 189
- Aedes aegypti*, i, 256, 257
- Alkalosis, i, 224
- Allbutt, Sir Thomas Clifford, death of, i, 223
- Anæsthesia, i, 300
 - preliminary injections of morphine and magnesium sulphate, i, 230
- Analgesic properties of diathermy, i, 96
- Anaphylaxis and asthma, i, 230
- Angina pectoris, operations for, i, 292
 - sympathectomy for, i, 261
- Appendicitis, morphine in, i, 31
 - treatment of, i, 25
- Arrhythmias, cardiac, i, 7
- Ashhurst, Astley P. C.: The motions of the larger joints, i, 74
- Asthma and anaphylaxis, i, 230
 - treatment of, i, 231
- Atropine action on kidney, i, 265
- Auricular flutter, i, 11
 - treatment of, i, 21
- Avian tuberculosis, i, 177
- Avitaminosis, i, 232

B

- Bacillus tumefaciens*, i, 248
- Bacteria, soil, action of, on plants, i, 229
- Bacteriophage, i, 233
- Balfour, Donald C.: Recent progress in surgery, i, 289
- Bell's treatment of cancer, i, 245
- Bile-duct, stricture of common, case of, i, 185
- Bilirubin, van den Bergh's reaction for, i, 298
- Bladder, exstrophy of, case of, i, 182
- Blood and lymph-tissues, radiotherapy of, i, 112
 - flow of, new method of measuring quantitatively, i, 229
 - sedimentation test of, i, 234

- Blood-dilution in the pathology and treatment of attacks of gout, i, 44
- Blood-pressure, effect of liver extract on, i, 235
- Body, anatomical positions of, i, 74
- Breast, pre-cancerous changes in, i, 244

C

- Cancer, i, 223, 228, 236 *et seq.*
 - cultivation of, *in vitro*, i, 245
 - curietherapy of, i, 276
 - cytology of, i, 238
 - diagnosis of, i, 246
 - irritation theory of, i, 249
 - lead treatment of, i, 245
 - of humerus, i, 207
 - of plants, i, 228
 - of œsophagus, i, 207
 - parasitic theory of, i, 247
 - parthenogenetic theory of, i, 249
 - sero-diagnosis in, i, 250
- Carbon-dioxide anæsthesia, i, 300
- Carbon-tetrachloride poisoning, i, 252
- Cardiac arrhythmias, diagnosis and treatment of, i, 7
- Cattell, Henry W.: Progress of medicine, i, 222
- Cerebellopontile angle tumors, total removal of, i, 291
- Chest, wounds of, massive collapse of lungs in, i, 140
- Chicken sarcoma, i, 236, 237
- Colheccystitis, case of, i, 184
- Cholecystography, i, 252
- Circumduction, definition of, i, 76
- "Circus movement," i, 15
- Clinical action of diathermy, i, 92
- Collapse, massive, of lungs, i, 136
- Collip's work on parathyroids, i, 270
- Colon, pistol-shot wound of, i, 214
- Coupal, James F.: Progress of medicine, i, 222
- Curare, i, 220
- Cushing, H. B.: The sequelæ of diphtheria, i, 1
- Cysts, ovarian, case of, i, 178
- Cytology of cancer, i, 238

D

- Death-rate in diphtheria, i, 1
 DeKraft, Frederic: The clinical action of diathermy, i, 92
 Dengue fever, transmission of, i, 255
 Department of diagnosis, i, 1
 of electrotherapeutics, i, 92
 of medicine, i, 126
 of physiotherapy, i, 92
 of progress of medicine, i, 222
 of surgery, i, 177
 of treatment, i, 1
 Development of psychiatric research, i, 52
 Devine operation for duodenal ulcer, i, 290
 Diabetes, "silent," i, 224
 Diagnosis and treatment of cardiac arrhythmias, i, 7
 department of, i, 1
 physical, importance of, i, 222
 Diathermy, clinical action of, i, 92
 in senile changes of brain, i, 100
 Diathesis, i, 223
 Diphtheria, heart stimulants and, i, 257
 immunization of, i, 257
 sequelæ of, i, 1
 Disease, Hodgkin's, i, 117, 126
 types of, i, 223
 Distemper in dogs, causative agent of, i, 229
 Diuresis produced by novasurol, i, 270
 Duodenal ulcer, case of, i, 186
 Devine operation for, i, 290
 surgical treatment of, i, 199
 Dwarfs, mongoloid, i, 268
 Dyes, therapeutic value of some, i, 258

E

- Eclampsia, kidney tests in, i, 277
 magnesium sulphate in, i, 275
 Ectopic pregnancy, leukocyte count in, i, 274
 Electricity, therapeutic value of, i, 258
 Electrotherapeutics, department of, i, 92
 Erysipelas treated by radiant light and heat, i, 109
 Ethmoiditis, chronic, diathermy in, i, 99
 Eversion, definition of, i, 76
 Ewes, milk secretion after insulin, i, 264
 Extrophy of bladder, case of, i, 182
 Extension, definition of, i, 76

F

- Family trees, diseases in, i, 223
 Fever, dengue, i, 255
 rat-bite, i, 280
 rheumatic, i, 280
 Rocky Mountain (tick), i, 229
 Fibromyomas of uterus, case of, i, 181
 Flexion, definition of, i, 76

- Flutter, auricular, i, 11
 treatment of, i, 21
 fibrillation, i, 12
 Fœtus, non-syphilitic diseases of, i, 276
 Folin's technic, i, 44
 Foot-and-mouth disease controlled, i, 229
 Forceps, influence of, on infant mortality, i, 279
 Foreign body inhalation, i, 141
 Fracture of humerus, pathological function of, i, 207
 Functional tests of, i, 266

G

- Gall-bladder, röntgenologic diagnosis of diseases of, i, 296
 Gastric ulcers, surgical treatment of, i, 199
 Germs, deadly, made harmless, i, 229
 Glycosuria-phloridzin test for diagnosis of pregnancy, i, 277
 Glycosuria, renal, i, 172
 Goniometer, i, 75
 Gonorrhœa, diagnosis of, i, 260
 Gonorrhœal infections treated by radiant light and heat, i, 108
 Gout, i, 223
 blood dilution in the pathology and treatment of attacks of, i, 44
 Gouty series, i, 223
 Granuloma, Hodgkin, i, 126
 Graves's disease, extra-systoles of heart in, i, 8
 Gwyn, Norman B.: Massive collapse of the lungs, i, 136
 Gye's discovery, i, 236
 Gynecology, contra-indications to use of radium in, i, 120

H

- Head, infections about, i, 107
 Heart, arrhythmias of, i, 7
 effect of diphtheria on, i, 257
 disorders of, i, 260
 premature beats of, i, 8, 9
 treatment of, i, 20
 Heart-block, i, 15, 18
 treatment of, i, 23
 Heat in treatment of disease, i, 92
 Hendricks, William A.: A day in Dr. Charles H. Mayo's Clinic, i, 177
 Hepatic extract, effect of, on blood-pressure, i, 235
 Heredity, i, 262
Herpetomonas donovani, i, 265
 Hodgkin granuloma, i, 126
 sarcoma, i, 126
 Hodgkin's disease, i, 117, 126
 Horgan, Edmund: Diagnosis and treatment of acute superficial circumscribed abscess, i, 189
 Humerus, pathological fracture of, i, 207

I

- Infection, treatment of local, i, 101
 Insulin, anaphylaxis from administration of, i, 263
 and milk secretion, i, 264
 intratracheal injections of, i, 263
 in pernicious vomiting of pregnancy, i, 264
 Intratracheal injection of insulin, i, 263
 Inversion, definition of, i, 76
 Irrigation, i, 264
 Ischæmia cordis intermittens, i, 260

J

- Jaundice, i, 225
 Jaundiced patients, preparation for operation, i, 299
 Jensen's rat sarcoma, i, 237
 Joints, motions of larger, i, 74
 Jourda, L. M.: Blood dilution in the pathology and treatment of attacks of gout, i, 44

K

- Kala-azar, i, 265
 Kidney function and nitrogen retention, i, 168
 pistol-shot wound of, i, 214
 Kidney-test in eclampsia, i, 277
 Knee, traumatic injuries of, i, 216, 219
 Kraepelin, E.: The development of psychiatric research, i, 52

L

- Laboratory methods, use and abuse of, i, 223
 Laroque, G. Paul: The treatment of appendicitis, i, 25
 Lead poisoning by tetrachloride of, i, 286
 treatment of cancer, i, 245
 Leiomyoma, use of radium for, i, 278
 Leukæmia, i, 126
 chronic myelogenous, i, 115
 lymphatic, i, 114
 Leukocyte count in diagnosis of ectopic pregnancy, i, 274
 Liver extract, effect of, on blood-pressure, i, 235
 functional tests of, i, 266
 rupture of, case of, i, 211
 Lungs, massive collapse of, i, 136
 Lymphatic leukæmia, i, 114
 Lymphogranulomatosis maligna, i, 126
 Lymphosarcoma, i, 116
 Lymph-tissues and blood, radiotherapy of, i, 112

M

- Magnesium sulphate, administration of, before anæsthesia, i, 230
 in treatment of eclampsia, i, 275

- Malaria in treatment of syphilis of the nervous system, i, 65, 272
 Manila, dengue fever of, i, 255
 Mason, Edward H.: The life history of a case of nephrosis, i, 163
 Massive collapse of lungs, i, 136
 Mayo, Charles H., Clinic of, 177
 William J.: Harrisburg address of, i, 223
 Medicine, art of, i, 222
 progress of, i, 222
 science of, i, 222
 Metasyphilitic disorders, treatment of, i, 63
 Milk secretion and insulin, i, 264
 ultra-violet light action on, i, 222
 Miller, C. Jeff.: Contra-indications to the use of radium in gynæcology, i, 120
 Mitral stenosis, operation for, i, 294
 Monogoloid dwarfs, i, 268
 Morphine, action on kidney, i, 265
 before anæsthesia, i, 230
 in appendicitis, i, 31
 Motions of larger joints, i, 74
 Muir, Joseph: Radiotherapy of the blood and lymph-tissues, i, 112
 Mumps, etiology of, i, 269
 Muscle testing in poliomyelitis, i, 273

N

- Nassau, Charles F.: The surgical treatment of gastric and duodenal ulcers, i, 199
 Nephrosis, life history of a case of, i, 163
 Nitrogen retention and healing function, i, 168
 Node, sino-auricular, i, 7
 Novasurol, diuretic action of, i, 270
 Nurses, training of, i, 227

O

- Oesophagus, "silent" growth of, i, 207
 Oils, action of, in producing tumors, i, 241, 243
 Olive oil, action of ultra-violet light on, i, 222
 Ophthalmia, purulent and gonorrhœal, i, 108
 Otitis media treated by radiant light and heat, i, 108
 Ovarian cysts, case of, i, 178

P

- "Pacemaker," i, 7
 Paraplegia, i, 126
 Parathyroid extracts, i, 270
 tetany, i, 272
 Paresis, malarial treatment of, i, 272
 Peptic ulcer, experimental, i, 290
 Pernicious vomiting of pregnancy treated by insulin, i, 264
 Pertussis, spirochæte, cause of, i, 269

- Phloridzin test for diagnosis of pregnancy, i, 277
- Phthisis, diathesis in, i, 223
- Physical diagnosis, importance of, i, 222
- Physicians, training of, i, 226, 227
- Physiotherapy, department of, i, 92
- Planes of body, i, 75
- Plants, cancer of, i, 228
- Plaut, F.: The treatment of metasyphilitic disorders of the nervous system with infectious diseases, in particular with relapsing fever, i, 63
- Plimmer's bodies, i, 241
- Pneumonia, diathermy in, i, 99
- Pneumography as an aid to diagnosis, i, 293
- Poisoning, carbon tetrachloride, i, 252
- Poliomyelitis, muscle testing in, i, 273
treatment of, i, 273
- Pregnancy, early diagnosis, by glycosuria-phloridzin test, i, 277
ectopic, leukocyte count in, i, 274
pernicious vomiting of, i, 264
- Progress of medicine, i, 222
- Pronometer, i, 82
- Psicaine, i, 279
- Psychiatrial research, development of, i, 52
- Purulent and gonorrhoeal ophthalmia, i, 108
- Pusey's remarks on training of physicians, i, 226
- R**
- Radiant light and heat in local infections, i, 103
- Radiotherapy of blood and lymph-tissues, i, 112
- Radium, i, 279
contra-indications to use of, in gynecology, i, 120
use of in cancer and leiomyoma of uterus, i, 278
- Rat sarcoma, i, 237
- Rat-bite fever, i, 280
- Raynaud's disease, operation for, i, 292
- Red, neutral, excretion of, by stomach, i, 286
- Reid, J. Spence: Recent progress in surgery, i, 289
- Reifenstein, Edward C.: The diagnosis and treatment of cardiac arrhythmias, i, 7
- References, abscess, acute, i, 198
massive collapse of lungs, i, 162
nephrosis, i, 176
progress of medicine, i, 287
radium, i, 118
surgical, i, 302
- Relapsing fever in the treatment of metasyphilitic disorders, i, 63
- Renal glycosuria, i, 172
- Rheumatic fever, i, 280
- Rheumatic series, i, 223
- Rickets, ultra-violet light in, i, 281
- Rocky Mountain spotted fever, vaccine
in treatment of, i, 229
- Rous chicken sarcoma, i, 236, 237
- Rotation, definition of, i, 76
- S**
- S.-A., i, 8
- Sarcoma, Hodgkin, i, 126
Jensen's rat, i, 237
Rous chicken, i, 236, 237
- Seasickness, treatment of, i, 284
- Sedimentation test of blood, i, 234
- Sequelæ of diphtheria, i, 1
- Sero-diagnosis in cancer, i, 250
- "Silent" cancer, i, 207
diabetes, i, 224
- Sino-auricular node, i, 7
- Sinus arrhythmia, treatment of, i, 20
- Sinusitis, treatment of, i, 110
- Smallpox, i, 223
- Snow, William Benham: Treatment of local infection, i, 101
- Sodium tetra-iodophenolphthalein in cholecystography, i, 252
- Soja hispida*, i, 233
- Spirochæta duttoni*, i, 65
- Spirochæta as cause of mumps, i, 269
- Spleen, i, 285
- Spotted fever, Rocky Mountain, treatment of, i, 229
- Stomach, excretion of neutral red by, i, 285
ulcers of, surgical treatment of, i, 199
- Surgery, department of, i, 177
recent progress in, i, 289
- Sympathectomy for angina pectoris, i, 261
- Syphilis of nervous system, treatment of, i, 63
- T**
- Tachycardia, i, 10, 11
treatment of, i, 21
- Test, sedimentation, i, 234
- Tetany, parathyroid, i, 272
- Tetrachloride of lead poisoning, i, 286
- Tetra-ethyl lead, i, 286
- Thrombo-angiitis obliterans, i, 284
- Tick fever, treatment of, i, 229
- Training of nurses, i, 227
of physicians, i, 226
- Treatment, department of, i, 1
of appendicitis, i, 25
of local infection, i, 101
- Tropical diseases, i, 223
- Tuberculosis, avian, i, 177
- Tumors, cerebellopontile angle, total removal of, i, 291

U

- Ulcer, duodenal, case of, i, 186
duodenal, Devine operation for, i, 290
peptic, experimental, i, 290
surgical treatment of, i, 199
gastric, surgical treatment of, i, 199
Ultra-violet light, action of, on milk, i, 222
in rickets, i, 281
on olive oil, i, 222
Uræmia, i, 226, 277
Urea, use of, in advanced heart failure, i, 261
Uterus, fibromyomas of, case of, i, 181

V

- Van den Bergh reaction for bilirubin, i, 298

Viscosimeter, i, 46, 50

Vitamin E, i, 229

Vomiting, pernicious, of pregnancy treated by insulin, i, 264

W

Weber, F. Parkes: Paraplegia in lympho-granulomatosis maligna (Hodgkin's disease) and leukæmia, and the question of there being a "Hodgkin sarcoma" as well as a "Hodgkin granuloma," i, 126

Wounds of chest, massive collapse of lungs in, i, 140

X

X-ray pictures, transmission by wire, i, 222

